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MGUS: Experts Identify Risk Factors For Disease Progression And Establish Monitoring Guidelines

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The International Myeloma Working Group, a group of leading myeloma doctors, recently published a report identifying risk factors for disease progression in patients with the multiple myeloma precursor diseases, monoclonal gammopathy of undetermined significance (MGUS) and smouldering myeloma. In addition, the myeloma experts established guidelines for the monitoring and management of these two conditions. This article, Part 1 in a series, covers the results for MGUS. Part 2 will cover the results for smoldering myeloma.

The International Myeloma Working Group (IMWG) identified the following risk factors for patients with MGUS: the amount of monoclonal protein, the type of monoclonal protein, the number of bone marrow plasma cells, and the free light chain ratio.

According to Dr. C. Ola Landgren, researcher at the National Institutes of Health and investigator in this study, approximately three million Americans have a myeloma precursor disease, such as monoclonal gammopathy of undetermined significance (MGUS) or smoldering myeloma, but only about 5 percent will develop multiple myeloma or a related disease.

He added that “at the same time, among those who will develop multiple myeloma, I think there is strong evidence to suggest that they all went through a precursor stage. So, the solution is to identify progressors from non-progressors at an early stage, and to deliver intervention (i.e. treatment) that will delay/prevent progression to full-blown disease.”

With their report, the IMWG aims to help doctors identify which patients may be at a higher risk for disease progression and provide guidelines to help monitor and manage their conditions.

MGUS Rates And Risk Factors

A previous study investigated a group of 21,463 people 50 years and older. The researchers identified 3.2 percent of the people as having MGUS.

The researchers found that the rate of MGUS increased with age. The condition was more common in men than women, and it was approximately twice as common in African-Americans and Africans compared to Caucasians. Furthermore, the occurrence of MGUS in first degree relatives with MGUS was higher, suggesting a genetic factor.

Of those diagnosed with MGUS, approximately 1.5 percent of patients progressed to multiple myeloma or a related disease each year.

The IMWG identified a number of risk factors to help doctors predict which MGUS patients may progress.

The most important risk factor of progression was the amount of the monoclonal (M) protein at the time of MGUS identification. In MGUS and multiple myeloma, the M-protein is overproduced by plasma cells and cannot effectively fight infections.

In one study, the risk of progression to multiple myeloma or a related disorder 20 years after the recognition of MGUS was 49 percent in patients with an M-protein value of 25 g/l compared to 14 percent for patients with an M-protein value of 5 g/l or less. MGUS patients with an increase in the amount of the M-protein during the first year after diagnosis were at high risk of disease progression.

The type of monoclonal protein overproduced in MGUS patients was also identified as a risk factor. There are several different types of M-protein. Each MGUS and myeloma patients overproduces just one type. Those patients with the IgM or IgA type of M-protein were found to be at increased risk of progression compared to those patients with too much IgG.

Additionally, the IMWG cited a report in which patients with greater than 5 percent bone marrow plasma cells were found to be at increased risk of progression.

Lastly, patients with abnormal free light chain ratios were found to be at significantly higher risk for progression than those with a normal ratio. In healthy individuals and the majority of myeloma patients, an immunoglobulin is composed of two light chains bound to two heavy chains. In some patients, the light chains are separated, creating abnormal “free” light chains in their blood stream.

Among MGUS patients with all of the high-risk factors (M-protein levels greater than 15 g/l, overproduction of IgM or IgA, and abnormal free light chain ratios) 58 percent progressed within 20 years of their MGUS diagnosis. For those with none of these factors present, 5 percent progressed.

MGUS Monitoring and Management Guidelines

The IMWG recommends that when a patient is diagnosed with MGUS, doctors should complete a full physical examination of the patient with emphasis on symptoms that may suggest multiple myeloma.

If blood work shows that the serum M-protein is low and of the IgG type and that the free light chain ratio is normal, patients should be categorized as low risk. In this scenario, patients should be monitored again in six months and, if stable, followed every two to three years until symptoms of multiple myeloma or a related disease appear.

If a patient with MGUS has a high M-protein level of IgA or IgM type and an abnormal free light chain ratio, the IMWG recommends a bone marrow biopsy be conducted to rule out multiple myeloma or a related disease. If results do not indicate an underlying plasma cell disorder, patients are considered intermediate or high risk. These patients should be monitored again in six months and then annually until symptoms of multiple myeloma or a related disease appear.