Monoclonal Gammopathy of Undetermined Significance (MGUS) Facts

Normal plasma cells (a type of white blood cell) produce antibodies (also known as immunoglobulins) which help fight infection. Each type of plasma cell produces only one type of immunoglobulin (Ig), the same immunoglobulin protein as the original abnormal cell. When a particular plasma cell is copied many times, this causes an excess amount of one type of immunoglobulin called monoclonal protein (M protein). Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic condition in which there is a presence of an abnormal M protein in the blood. It is not a blood cancer, and most people with MGUS do not ever develop a blood cancer. However it is important that the condition be monitored, since increasing levels of this protein in addition to other tests may indicate a risk of progression to smoldering myeloma, myeloma, lymphoma, light-chain amyloidosis or Waldenstrom macroglobulinemia.

There are two kinds of MGUS. The lymphoid type which secretes immunoglobulin M (IgM) and may progress to Waldenstrom macroglobulinemia, lymphoma or other malignant lymphoproliferative disorders. The other type, plasma cell MGUS or non IgM (IgG, IgA, Ig light chain only, IgD or IgE), may progress to myeloma or related plasma cell disorders. The type that most commonly progresses to myeloma is IgG.

Symptoms and Risk Factors

MGUS does not typically cause any symptoms. There is no evidence of bone damage, kidney damage, anemia (low levels of red blood cells), or elevated calcium levels. The average risk of progression to multiple myeloma is one percent per year. The risk of progression to malignancy is about 20 to 25 percent of people during their lifetime.

It has always been recognized that some cases of MGUS progressed to symptomatic multiple myeloma but recent studies have shown that multiple myeloma is consistently preceded by MGUS.

The prevalence of MGUS is higher in African-Americans. Other risk factors are age, male sex, exposure to pesticides and family history of MGUS or myeloma.

Diagnosis

MGUS is usually detected following a routine blood test. An initial follow-up appointment six months after the diagnosis is common for most people with MGUS. An assessment of risk

factors can be used to help determine the risk of progression to myeloma and the necessary frequency of monitoring. If the risk is low, less frequent follow-up will be recommended.

The doctor will be looking for a blood M protein level of less than 3 grams per deciliter and a bone marrow plasma cell level of less than 10 percent. He or she will also look for evidence of other B-cell disorders.

Diagnosing MGUS

- M spike less than 3 grams per deciliter
- Marrow plasma cells less than 10 percent
- No CRAB criteria: C—Calcium elevation (high levels of calcium in the blood; also known as "hypercalcemia"); R—Renal insufficiency (poor function of the kidneys that may be due to a reduction in blood-flow to the kidneys); A—Anemia (low red blood cell counts); B—Bone abnormalities (lesions).

MGUS Monitoring and Management Guidelines

The International Myeloma Working Group (IMWG) recommends doctors should complete a full physical examination of the patient with emphasis on symptoms that may suggest multiple myeloma. Blood work should also be done.

Low Risk: If the 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 followed with a serum protein electrophoresis test at six months and, if stable, followed every two to three years until symptoms of multiple myeloma or a related disease appear.

Immediate or High Risk: 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 with a serum protein electrophoresis test again in six months and then annually until symptoms of multiple myeloma or a related disease appear.

As more is understood about the progression of MGUS to myeloma and other blood cancers, there is greater understanding of these conditions. Research studies are being done to determine the risk of progression more clearly and to see if the high risk group of patients might benefit from treatment. Currently there is no treatment indicated for MGUS outside of a clinical trial.

Related Disease- Smoldering Myeloma

Smoldering multiple myeloma (SMM) is also an asymptomatic disorder; however, it carries a risk of progression to myeloma of 10 percent per year in the first five years. Testing should be done 2–3 months after the initial recognition of SMM. If the results are stable, the patient should be followed every 4–6 months for 1 year and, if stable, every 6–12 months.

Certain factors such as the presence of deletion 17p or a translocation between chromosome 4 and 14 seem to be associated with the shorter time to progression. Also bone lesions which may not be seen on a skeletal survey, but may be seen on a PET scan, CT scan or MRI may indicate higher risk disease, or possibly the need to start treatment.

There are some clinical trials for smoldering myeloma to try to determine if some high risk cases might benefit from early treatment.

Diagnosing Smoldering Myeloma

- M spike of greater than or equal to 3 grams per deciliter
- Or urinary M protein greater than 500 milligrams per 24 hours and/or
- Marrow plasma cells greater than or equal to 10 percent
- No CRAB criteria: C—Calcium elevation (high levels of calcium in the blood; also known as "hypercalcemia"); R—Renal insufficiency (poor function of the kidneys that may be due to a reduction in blood-flow to the kidneys); A—Anemia (low red blood cell counts); B—Bone abnormalities (lesions).

Acknowledgement

LLS gratefully acknowledges

Matthew Lunning, DO
Assistant Professor
University of Nebraska Medical Center
Omaha, NE

for his review of *Monoclonal Gammopathy of Undetermined Significance (MGUS) Facts* and his important contributions to the material presented in this publication.

We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the United States and in Canada. To find the chapter nearest to you, visit our website at www.LLS.org or contact

The Leukemia & Lymphoma Society
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Contact an Information Specialist at (800) 955-4572
Email: infocenter@LLS.org

LLS offers free information and services for patients and families touched by blood cancers. The following lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They can answer general questions about diagnosis and treatment options, offer guidance and support and assist with clinical-trials searches. Language services are available. For more information, please

- Call: (800) 955-4572 (Monday - Friday, 9 a.m. to 9 p.m. EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org
- Visit: www.LLS.org/informationspecialists.

Free Materials. LLS offers free education and support publications about myeloma, clinical trials, lab and imaging tests and other blood cancer-related topics that can be either read online or downloaded. Free print versions can be ordered. For more information, please visit www.LLS.org/publications.

Clinical Trials (Research Studies). New treatments for patients with MGUS are under way. Patients can learn about clinical trials and how to access them. For more information, please

- Call: (800) 955-4572 to speak with our LLS Information Specialists who can help conduct clinical trial searches
- Visit: www.LLS.org/clinicaltrials.

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