Multiple Myeloma - Staging

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Stages

Staging is a way of describing where a cancer is located, if or where it has spread, and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the cancer's stage, so staging may not be complete until all of the tests are finished. Knowing the stage helps the doctor to decide what kind of treatment is best and can help predict a patient's prognosis (chance of recovery). There are different stage descriptions for different types of cancer.

In myeloma, it is important to begin with whether the patient is experiencing symptoms. It is common to classify patients with newly diagnosed myeloma as being either symptomatic from the disease (having symptoms and signs) or asymptomatic (without any symptoms). Patients without symptoms are generally watched closely without treatment, which is called active surveillance (see Treatment [2]). Patients with symptoms need treatment.

As described below, the symptoms related to the myeloma include hypercalcemia (elevated blood **C**alcium), poor **R**enal or kidney function, **A**nemia, or **B**one pain or bone lesions (CRAB).

- **C**alcium levels increased: serum calcium > 0.25 mmol/l above the upper limit of normal or > 2.75 mmol/l
- **R**enal insufficiency: creatinine > 173 mmol/l
- **A**nemia hemoglobin 2 g/dl below the lower limit of normal or hemoglobin < 10 g/dl
- **B**one lesions; lytic lesions or osteoporosis (thinning of the bones) with compression fractures (an MRI or CT test may clarify)
- Other: symptomatic hyperviscosity, amyloidosis [3], and/or recurrent bacterial infections (more than 2 episodes in 12 months)

The Durie-Salmon system had traditionally been used for the staging of myeloma. This staging system is good for assessing the extent of the disease or size of the tumor. According to this system there are three stages; each stage is further subclassified into A or B depending on whether kidney function has been affected (with the subclassification B meaning there is significant kidney damage).

However, another classification system called the International Staging System (ISS) is now used more commonly. It defines the factors that influence patient survival. The ISS is based on data collected from patients with multiple myeloma from around the world. The system has three stages based on the measurement of serum albumin and the levels of serum ?2-M. Recent efforts involve further classifying myeloma based upon patterns of gene expression in myeloma cells; this is an ongoing area of research.

Stage I

Many patients with stage I myeloma show no symptoms because there are fewer cancer cells in the body. If the cancer has affected kidney function, the prognosis may be worse regardless of the stage. Factors characteristic of stage I include:

Durie-Salmon system

- Number of red blood cells within or slightly below normal range
- Normal amount of calcium in the blood
- Low levels of M protein in the blood or urine
- No bone damage on x-rays

ISS

- ?2-M less than 3.5 grams per deciliter (gm/dL)
- Albumin greater than or equal to 3.5 gm/dL

Stage II

Durie-Salmon system

More cancer cells are present in the body in stage II. Again, if kidney function is affected, then the prognosis worsens regardless of the stage. Criteria for stage II are defined as those that fit neither stage I nor stage III.

ISS

- ?2-M greater than 3.5 gm/dL, but not greater than 5.5 mg/dL, and/or
- Albumin less than 3.5 gm/dL.

Stage III

Many cancer cells are present in the body at stage III. Factors characteristic of this stage are:

Durie-Salmon system

- Anemia with a hemoglobin less than 8.5 gm/dL
- Hypercalcemia
- Advanced bone damage (more than three bone lesions)
- High levels of M protein in the blood or urine, which is defined as:
  - Immunoglobulin G (IgG; an antibody in the blood that fights infection) value greater than 7 gm/dL
  - IgA (Immunoglobulin A; another specific type of antibody) value greater than 5 gm/dL
  - Urine light chain M component on electrophoresis greater than 12gm/24h. This is a type of protein that is usually cleared from the blood through the kidneys and then reabsorbed. If this is found in the urine, it could indicated multiple myeloma, and electrophoresis is the method that laboratory uses to identify and classify it.

ISS

- ?2-M greater than 5.5 gm/dL

Recurrent myeloma: Myeloma that returns after a period of being in control after treatment is called recurrent myeloma or relapsed myeloma. If there is a recurrence, the cancer may need to be staged again (called re-staging) using the system above.

Other classifications

Some people have no symptoms of myeloma, but they may have abnormal plasma cells producing an abnormal protein (M protein). Doctors generally monitor these people closely, and active treatment does not begin unless this condition turns into symptomatic myeloma.

Monoclonal gammopathy of unknown significance (MGUS)

This condition occurs when people have a low level of M protein (meaning there are small quantities of abnormal plasma cells), but they do not have any other evidence of myeloma, such as bone damage, excessive plasma cells, or low numbers of red blood cells. People with MGUS have a 1% chance per year of developing myeloma or lymphoma [4]. For this reason, doctors monitor the health of people with MGUS on a regular basis.

Smoldering multiple myeloma (SMM) or asymptomatic myeloma

People who are diagnosed with SMM have slightly higher levels of M protein and more plasma cells in the bone marrow than people with MGUS. There is still no evidence of symptoms or signs of myeloma, such as bone disease or anemia. But, a person with SMM may be prescribed bisphosphonates for symptoms of osteoporosis or osteopenia (a low density of bone minerals). Most people with SMM eventually develop myeloma. For this reason, doctors closely monitor the health of people with smoldering myeloma.

Prognosis

The International Staging System (ISS) of myeloma gives information about prognosis and predicts the person?s chance of recovery. Researchers are also looking at other ways to predict prognosis for patients with multiple myeloma. Some of these ways of evaluating prognosis include:

- High levels of ?2-M may indicate a large number of myeloma cells are present and kidney damage has occurred. The level of this protein increases as myeloma becomes more advanced.
- Lower amounts of serum albumin may indicate a poorer prognosis.
- Lactase dehydrogenase (LDH) is an enzyme; higher blood levels of LDH indicate a poorer prognosis.
- Abnormalities of chromosomes in the cancer cells may show how aggressive the cancer is.
- A plasma cell labeling index can be done in a specialized laboratory using bone marrow samples to find out how fast the cancer cells are growing.

Learn more about talking with the doctor about prognosis [5].

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/19374
[3] http://www.cancer.net/node/18450
[4] http://www.cancer.net/node/19207
[5] http://www.cancer.net/node/24394