UAMS myeloma institute

Information on AL AMYLOIDOSIS

What is AL Amyloidosis?

When an abnormal protein builds up in a tissue or organ, it is referred to as Amyloid and the disease it causes, Amyloidosis. Amyloid protein fibers can collect in any tissue or organ, including the kidneys, heart, liver or spleen.
Amyloid deposits can be generalized and be at several places in the body, or localized, meaning that they gather in only one specific area of the body.

Types of Amyloidosis

There are several different types of amyloid, however, the three most common types are Amyloid Light Chain (AL), Amyloid Serum A Protein (AA, also known as SAA), and Amyloid Transthyretin (ATTR) which is a hereditary condition.

In the United States, AL amyloidosis is the most common type, with about 4,500 new cases diagnosed each year.

AL amyloidosis is caused by a bone marrow disorder where the bone marrow, in the center of bones, produces abnormal plasma cells. These abnormal plasma cells normally produce antibodies, also called immunoglobulins. These antibodies are an essential part of the immune system that protects the body from infection. They are composed of four protein chains: two light chains, either kappa or lambda, and two heavy chains.

In AL amyloidosis, the plasma cells grow out of control as a single cell type and make abnormal antibodies. The abnormal antibodies enter the blood stream and are deposited as amyloid protein in tissue or organs.

AL usually affects people between the ages of 50 and 80 and is more common in males than in females, 70% versus 30%.

Symptoms

Amyloid protein is deposited in different organs and sites and affects the performance of the site where it is deposited. Depending on which organs are affected and the degree to which organ function is affected, symptoms of AL amyloidosis will vary. Initially, the symptoms can be minor and similar to those of many other conditions. They can come on quickly and be severe. Fatigue, weight loss and swelling, however, are the most common symptoms.

Organ-Specific Symptoms:

- **Kidneys**

Kidney disease is common in patients with AL amyloidosis. Amyloid deposits in the kidneys can affect how toxins are filtered from the blood. This abnormality of the kidneys may result in a condition called nephrotic syndrome, characterized by excess protein in the urine and significant swelling in the lower legs. In some cases, the amyloid deposits cause

the kidneys to lose the ability to purify the blood, which can lead to kidney, or renal, failure. Patients with renal failure might need dialysis.

Heart

Amyloidosis in the heart can cause it to become thick and stiff, making it unable to function efficiently. This results in shortness of breath, even with just minor exertion. It can also affect the electrical system of the heart, resulting in abnormal heart beat - a speeding up or slowing down of the heartbeat.

Digestive System

Amyloidosis in the digestive system can cause nausea, diarrhea or constipation, weight loss, loss of appetite, or a feeling of fullness in the stomach after eating small amounts. Sometimes the tongue can appear swollen.

Nervous System

Amyloidosis can affect nerves in the hands, feet and lower legs, causing pain, numbness, tingling, and loss of sensitivity to temperature. This condition is known as *peripheral neuropathy*. Nerves that control blood pressure, heart rate and other body functions can also be affected, causing a variety of symptoms, including dizziness when standing too quickly, nausea and diarrhea. This is known as *autonomic neuropathy*.

Other Symptoms

Other symptoms that may be present for a period of time prior to diagnosis include chronic fatigue, weakness, weight loss, bruising around the eyes and other areas of skin folds, and swelling in joints.

Diagnosis

Diagnostic testing for AL amyloidosis involves blood tests, urine tests and biopsies. Blood and/or urine tests can indicate signs of the amyloid protein, but only bone marrow tests or biopsies of affected tissues or organs can positively confirm the diagnosis. Some tests are done only once to establish a diagnosis, while others are repeated periodically to monitor disease progression and response to treatment.

Diagnostic tests are done in order to

- **Establish a diagnosis and the extent of the amyloid**
- **Develop a treatment plan and monitor progress**
- **Identify complications so they can be managed and prevented**

Blood and Urine Tests

Blood and urine are analyzed to detect the abnormal protein produced by the bone marrow plasma cells.

The serum Free Light Chain Assay is done to detect changes in the level of free light chains in the blood, which is an indicator of changes in disease activity. Free light chain measurements are done regularly to assess how well treatment is working and to confirm that the amyloid is stable during periods off treatment.

Biopsy of the affected organ and/or bone marrow

A biopsy involves the removal of a small sample of tissue to look for evidence of amyloid deposit via microscopic examination. A sample can be taken from an organ, such as the heart or kidneys, from the rectum, or from fat pads under the skin in the abdomen.

There are two types of bone marrow tests that may be performed: a bone marrow aspirate (removal of liquid bone marrow) and a bone marrow biopsy (removal of a 1 to 2 cm core of bone marrow tissue). These tests help determine the percentage of amyloid-producing plasma cells which helps guide treatment.

Echocardiogram and Imaging

An echocardiogram of the heart can identify amyloid deposits in the heart and the extent of the amyloid's impact. The serum BNP is a good marker of heart function. Heart MRI is the definitive imaging method to identify amyloid in the heart.

Treatment

The goal of treatment for AL amyloidosis is to reduce the abnormal light chain to zero or close to zero to prevent progression of the disease.

Treatments may include:

- **Dose adjusted Autologous Stem Cell Transplantation** is the standard approach for treatment and gives the best responses that are stable for the longest periods of time. Steroids, such as dexamethasone, are used to trigger destruction of abnormal plasma cells.

- **Thalidomide or Revlimid® (lenalidomide),** are immunomodulatory drugs that enhance the activity of cells in the immune system against the abnormal plasma cells.

- **Velcade® (bortezomib),** a proteasome inhibitor, is used to kill tumor cells.

- **Chemotherapy,** typically with Melphalan or Cyclophosphamide, is used to control the growth of abnormal plasma cells that produce amyloid.

Supportive Treatment

Supportive treatment is helpful for various symptoms, including cardiac and kidney problems, and can improve quality of life.

Doctors can prescribe medications and treatments, including:

- **Special diet, such as a low-salt diet**
- **Anti-nausea medication**
- **Medication to relieve fluid retention**
- **Blood-thinning medication**
- **Blood pressure medication**
- **Dialysis if kidney function is severely compromised**

It is important for a patient to consult with a specialist who is knowledgeable about the treatment of amyloid patients.

Prognosis

Complete remission, defined as the absence of light chains in the blood, occurs in about 60% of patients. Although organ function can improve in 30%–40% of patients after treatment, organ recovery is slow and depends on which organs are affected and how long the damage has been occurring. If treatment begins during the early onset of clinical symptoms, the overall success rate is higher.

Severe amyloidosis can lead to life-threatening organ failure.

A multi-disciplinary approach is essential. At the Myeloma Institute, the physician team includes myeloma specialists who also treat AL amyloidosis, nephrologists, cardiologists and other specialists as needed.

Every patient's disease is different. The Myeloma Institute physicians are dedicated to defining the nuances of each individual's disease and customizing treatment regimens that have the most promise for effective results.

This information about AL Amyloidosis and other patient education materials are available at www.myeloma.uams.edu