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## **Multiple Myeloma-Associated Amyloidosis – What Every Patient Should Know**

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During the course of their disease, multiple myeloma patients may develop a condition called amyloidosis. Amyloidosis is a disease in which proteins accumulate in organs such as the heart or kidneys, leading to organ damage and complications associated with some multiple myeloma treatments.

The following article describes amyloidosis as it relates to multiple myeloma and includes some of the current treatment recommendations for patients with this dual diagnosis.

### **What Is Amyloidosis?**

Amyloidosis occurs when proteins accumulate in organs such as the heart, kidney, liver, or intestines.

There are three major types of amyloidosis: primary, secondary, and hereditary. Each type of amyloidosis is classified by its underlying causes and the type of protein that accumulates in organs.

Primary amyloidosis is the most common form of amyloidosis and the only form that occurs with multiple myeloma. It is caused by fragments of abnormal antibodies (called light chains). These light chains stick to one another and accumulate in organs throughout the body. Although the exact cause of primary amyloidosis is unknown, the disease starts in the bone marrow.

Secondary amyloidosis is caused by a chronic infection or inflammatory disease such as rheumatoid arthritis. Treatment of the underlying chronic infection or inflammatory disease can slow or stop the progression of this type of amyloidosis.

Hereditary amyloidosis is a rare type of the disease and the only type that is inherited. Most commonly, a mutation of a protein made in the liver leads to protein accumulation in organs for this type of amyloidosis.

### **Occurrence Of Multiple Myeloma-Associated Amyloidosis**

Multiple myeloma is a cancer of the plasma cells. These cells are an important part of the immune system responsible for the production of antibodies, which are one of the body's first

defenses against infection. In multiple myeloma, the plasma cells overproduce one type of abnormal antibody.

The overproduction of abnormal antibodies puts myeloma patients at risk for developing amyloidosis.

Not all multiple myeloma patients will develop amyloidosis. "Every light chain is a little different," explained Dr. Rafael Fonseca of the Mayo Clinic.

He added that patients with amyloidosis have light chains with a shape that make them more prone to stick to one another.

It is estimated that 10 to 15 percent of multiple myeloma patients will experience symptoms from the development of amyloidosis during the course of their disease. However, as many as 38 percent of myeloma patients may develop amyloidosis but experience none of its symptoms.

## **Symptoms**

The symptoms of amyloidosis depend upon which organs are involved and how much protein has accumulated in them.

One of the hallmark symptoms of amyloidosis is swelling of the tongue. This is caused by the accumulation of light chains in the intestine and digestive system. Accumulation in the intestine can also cause a loss of appetite, diarrhea, and chronic nausea.

The nervous system is also a common site of protein accumulation. Resulting nerve damage can cause carpal tunnel syndrome (pressure on the median nerve in the wrist), another characteristic symptom of amyloidosis in multiple myeloma patients.

Other symptoms involving the nervous system include tingling, prickling, and numbness in the upper and lower extremities.

An additional symptom unique to amyloidosis is bruising around the eyes. This can occur when proteins accumulate in the tissues that connect, support, or surround other structures and organs of the body.

Other common symptoms include fatigue, weight loss, shortness of breath, swelling of the legs, and enlargement of the liver.

Researchers note, however, that the presence of symptoms alone is not enough to diagnose amyloidosis.

In order to confirm the diagnosis, a fine needle abdominal fat pad biopsy, rectal mucosa biopsy, or a bone marrow biopsy must be performed, and patients must meet the criteria defined by chemical testing of the biopsy.

## Treatment

Treatment for amyloidosis is aimed at reducing or eliminating the plasma cells that are responsible for the production of the abnormal light chain proteins. Such treatment reduces the accumulation of light chains throughout the body, which can alleviate some of the symptoms associated with amyloidosis.

Treatment for amyloidosis is similar to treatment for multiple myeloma. “Currently, many treatments can be used for both [multiple myeloma and amyloidosis]” said Dr. Fonseca.

Patients typically receive high-dose chemotherapy and a stem cell transplant.

Patients who are not eligible for stem cell transplantation may receive oral melphalan and prednisone (MP). They may also be treated with intravenous chemotherapy in the form of medium- or high-dose melphalan or vincristine-doxorubicin-cyclophosphamide.

The use of Velcade (bortezomib) and Revlimid (lenalidomide) for the treatment of amyloidosis is currently being studied. Initial trial results suggest that these drugs are effective for the treatment of amyloidosis patients.

The treatment of amyloidosis is, however, more challenging than treatment for multiple myeloma due to the associated organ damage. Particularly unfavorable from a treatment standpoint is damage to the heart and kidneys.

When considering the dual treatment of multiple myeloma and amyloidosis, complications due to organ involvement must be taken into account.

To date, research on the simultaneous treatment of amyloidosis and multiple myeloma has been focused mainly on special considerations regarding induction and high-dose melphalan therapies.

## Induction Therapy

A patient’s first treatment regimen of chemotherapy drugs is called induction therapy. The goal of induction therapy is to control the myeloma, reduce tumors, and enhance stem cell collection for transplantation.

According to a study published in Bone Marrow Transplantation, in patients diagnosed with amyloidosis alone, induction therapy has been shown to provide no additional benefit prior to stem cell transplantation than transplantation alone.

In fact, delaying the transplant by nine weeks for induction therapy prevented 13 percent of patients from continuing to transplant due to progression of their amyloidosis, ultimately resulting in death.

Based on this study, current recommendations suggest physicians treat myeloma-associated amyloidosis patients directly with stem cell transplantation.

If induction therapy is needed to reduce tumors prior to stem cell collection, it is recommended that patients receive a short course of dexamethasone. It is further cautioned not to delay stem cell transplantation to achieve maximal or complete response during induction therapy.

### **High-Dose Melphalan Treatment**

Currently, high-dose melphalan treatment given in combination with stem cell transplantation is the treatment of choice for selected myeloma patients. Damage to organs in amyloidosis patients, however, puts them at higher risk for treatment complications, which may result in death.

Some studies report that as many as 45 percent of amyloidosis patients may experience life-threatening complications resulting from high-dose melphalan therapy and stem cell transplantation, as compared to less than 2 percent of multiple myeloma patients.

It is known that patients with amyloidosis alone may require a reduction in melphalan dosage if they have heart involvement or damage to more than two organs. In these patients, the conventional melphalan dosage of 200 mg/m<sup>2</sup> may result in life-threatening complications following stem cell transplantation.

Often, multiple myeloma patients with amyloidosis are excluded from clinical trials. As a result, little is known regarding the response of these patients to novel agents. In order to get a full understanding of this unique subset of patients, researchers stress that it will be important to include them in clinical trials moving forward.

### **Amyloidosis Support Groups**

Those battling amyloidosis can feel overwhelmed and isolated by the diagnosis of the rare disease. A co-founder of the Canadian Amyloidosis Support Network (CASN) obtained much support from the Toronto Multiple Myeloma Support Group when she was diagnosed. With one-tenth the number of patients having amyloidosis, she knew the importance of making connections with others affected by this disease.

To date, Canadian amyloidosis patients have had the opportunity to gather in Toronto, Calgary and Vancouver. Information and support can be found on the CASN website [www.thecasn.org](http://www.thecasn.org) or by calling the toll-free number 1-877-303-4999.