UAMS myeloma institute

Information on WALDENSTROM MACROGLOBULINEMIA

What is Waldenstrom Macroglobulinemia?

Waldenstrom macroglobulinemia (Waldenstrom's) is a cancer of B lymphocytes (a type of white blood cell) that starts in the immune system.

Immune system cells make up the lymphoid tissue that is present throughout the body and that helps protect the body from infection. The main cells of lymphoid tissue are referred to as lymphocytes.

There are two main types of lymphocytes.

B lymphocytes (B cells) respond to an infection by changing into plasma cells. Plasma cells make proteins known as antibodies or immunoglobulins that help the body attack and kill disease-causing germs like bacteria. **T lymphocytes (T cells)** help direct immune responses and also can directly kill invading germs.

In Waldenstrom's, one of the B cells transforms into a cancer cell, which then multiplies out of control. Waldenstrom's cells can grow in the liver, spleen and lymph nodes, causing them to swell. They can also grow in the bone marrow, crowding out normal cells. When this happens, levels of red blood cells (which carry oxygen through the body) and white blood cells (which help the body fight infection) may fall. Levels of platelets, a type of blood cell that is responsible for clotting and stopping bleeding, also may fall.

A feature of Waldenstrom's is the overproduction by B cells of a protein called monoclonal immunoglobulin M (IgM, or macroglobulin) antibody, which circulates in the blood. The buildup of IgM can cause the blood to become too thick. This is called hyperviscosity. It can make it harder for blood to flow through small blood vessels and can cause symptoms of Waldenstrom's, such as problems with vision and the nervous system.

The cancer cells of Waldenstrom's are similar to those of two other types of cancer: multiple myeloma and non-Hodgkin lymphoma. Multiple myeloma is a cancer of plasma cells; non-Hodgkin lymphoma is a cancer of lymphocytes. Waldenstrom's cells have features of both plasma cells and lymphocytes; Waldenstrom's is a lymphoplasmacytic lymphoma.

Key Statistics

- Waldenstrom's is rare. About six people per one million are diagnosed each year in the United States; between 1,000 and 1,500 people are diagnosed annually.

- The chance of developing Waldenstrom's increases with age. Waldenstrom's mainly strikes individuals age 65 and older and most often affects white males.

- It is considered a low-grade, or indolent, lymphoma; it spreads slowly and can be well-controlled when diagnosed early.

Causes

No definite cause for Waldenstrom's has been identified. However, environmental, familial, genetic, and viral factors might play a role. About one in five people with Waldenstrom's has a close relative with Waldenstrom's or a related B-cell disease, such as MGUS (monoclonal gammopathy of undetermined significance) or some types of lymphoma or leukemia.

Certain changes in the DNA inside normal lymphocytes can cause them to become lymphoma or multiple myeloma cells. Changes in the DNA of some lymphoma cells can also cause them to produce high levels of IgM, leading to symptoms of Waldenstrom's. The DNA changes in Waldenstrom's cells are usually acquired after birth, versus being passed on from a parent. They often occur for no clear reason.

Waldenstrom's cells frequently have a mutation in a gene (genes are comprised of DNA) known as MYD88, which normally helps immune system cells signal each other and helps keep them alive. It is possible that the DNA change in this gene might make it stay turned "on" all the time, helping the Waldenstrom's cells survive longer than they should. Myeloma Institute scientists are investigating the factors that cause some genes to stay "on" and others to stay "off."

Symptoms

The overgrowth of B cell lymphocytes in Waldenstrom's inhibits the growth of normal cells, resulting in low numbers of red blood cells, white blood cells, and platelets, which can lead to fatigue, frequent infections and excessive bruising or bleeding. The abnormal lymphocytes also grow in the liver and spleen, which can cause the organs to become enlarged and result in abdominal pain.

Symptoms of Waldenstrom's can include:

- **Fatigue**
- **Bleeding of the gums**
- **Nose bleeding**
- **Blurred or decreased vision**
- **Dizziness, headache, confusion**
- **Easy bruising of the skin**
- **Numbness or tingling in the hands or feet**
- **Weight loss**
- **Fever and night sweats**
- **Swollen lymph nodes**
- **Heart palpitations**
- **Swelling in the feet and legs**
- **Abdominal pain**

It is possible for a person to be asymptomatic and yet, based on high levels of IgM, be diagnosed with Waldenstrom's. Sometimes Waldenstrom's produces few symptoms and develops slowly.

Diagnosis

The presence of IgM protein in the blood is a characteristic feature of Waldenstrom's. It is often discovered when a person goes to the doctor because of overt symptoms or just not feeling well. Sometimes it is found in people without symptoms who have blood work done for other reasons.

A diagnosis of Waldenstrom's is confirmed by performing a bone marrow or lymph node biopsy to determine whether abnormal lymphocytes are present. Additionally, specialized blood tests, such as serum protein electrophoresis, and urine tests are used to detect IgM protein and low blood cell counts.

Molecular genetic tests might be done to look for specific chromosome or gene changes.

Treatment

Treatment is based on an individual's symptoms and complications. Selection of treatment may be affected by factors such as age, general health and the type of symptoms. Not everyone with Waldenstrom's needs to be treated right away. Often, people who do not have serious or bothersome symptoms can be watched closely and then treated later, if needed.
If treatment is needed, there are several options.

- **Chemotherapy,** including chlorambucil (Leukeran), cladribine (Leustatin), cyclophosphamide (Neosar), and fludarabine (Fludara), alone or in various combinations

- **Monoclonal antibodies,** including Rituxan® (rituximab), which attaches to proteins on the surface of lymphoma cells and causes the cells to die

- **Biological therapies** designed to develop antibodies that destroy tumor cells

- **Proteasome inhibitors,** such as Velcade® (bortezomib) or Kyprolis®(carfilzomib)

- **Immunomodulating drugs (IMiDs),** such as Thalomid® (thalidomide), Revlimid® (lenalidomide), and Pomalyst® (pomalidomide) that alter the environment of the tumor cells, prompting them to die

- **Targeted therapies** that use small molecules to block pathways that enable cells to survive and multiply

- **Plasmapheresis (plasma exchange)** to lower blood viscosity caused by high levels of IgM

- **High-dose chemotherapy** with stem cell transplantation

- **Radiation therapy** to shrink enlarged spleen or lymph nodes if they are causing problems

Most patients can be treated on an outpatient basis. Physical examinations, routine blood chemistry evaluations and tests for serum paraprotein level, serum viscosity and coagulation are performed periodically to monitor for disease progression and to aid in treatment decisions.

It is important for patients and doctors to discuss all possible treatment options and related side effects in order to make the best decision that suits each individual's needs. No single treatment works for all patients. If the first drug or set of drugs does not work effectively, other drugs can be tried.

Prognosis

Duration of survival for Waldenstrom's patients has increased over the years, with reported median survival of up to 20+ years. Survival rates are based on reported outcomes of large numbers of people, but they cannot be used alone to predict the likely outcome for any particular person, since each person's cancer responds differently to treatment. It is important that patients speak with their doctors about their specific situations.

Future

In recent years, much progress has been made with the development of new drugs that work effectively. Ongoing scientific research is bringing about advanced, targeted treatment options and improved outcomes.

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

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