Waldenström's Macroglobulinemia: Questions and Answers

Key Points

- Waldenström's macroglobulinemia is a rare type of slow-growing, non-Hodgkin's lymphoma (cancer that begins in the cells of the immune system). It causes over-production of a protein called monoclonal macroglobulin (IgM) antibody (see Question 1).
- Symptoms include weakness, swollen lymph nodes, severe fatigue, nose bleeds, weight loss, and visual and neurological problems; some patients do not have symptoms (see Question 4).
- Waldenström's macroglobulinemia is diagnosed using bone marrow biopsy and blood tests; other techniques may also be used (see Question 5).
- Treatments for Waldenström's macroglobulinemia in patients with symptoms may include plasmapheresis, chemotherapy, and/or biological therapy (see Question 6).
- People with Waldenström's macroglobulinemia are encouraged to enroll in clinical trials (research studies with people) that explore new treatments (see Question 7).

1. What is Waldenström's macroglobulinemia?

Waldenström's macroglobulinemia (WM) is a rare, indolent (slow-growing) non-Hodgkin's lymphoma (cancer that begins in the cells of the immune system). WM is also called lymphoplasmacytic lymphoma. It starts in plasma cells, which develop from white blood cells called B lymphocytes or B cells.

B cells are an important part of the body's immune system. They form in the lymph nodes, spleen, and other lymphoid tissues, including bone marrow (the soft, spongy tissue inside bones). Some B cells become plasma cells, which make, store, and release antibodies. Antibodies help the body fight viruses, bacteria, and other foreign substances.

In WM, abnormal plasma cells multiply out of control, producing large amounts of a protein called monoclonal macroglobulin (IgM) antibody. High levels of IgM in the blood cause hyperviscosity (thickness or gumminess), which leads to many of the symptoms of Waldenström's (see Question 4).

2. How often does Waldenström's macroglobulinemia occur?

WM is a rare cancer, with about 1,500 new cases annually in the United States. The incidence of WM is higher in males and higher in whites than in African Americans. Incidence increases sharply with age. The median age at diagnosis is 63 (half of the cases are diagnosed before age 63, and half are diagnosed after age 63) (1).

3. What are the possible causes of Waldenström's macroglobulinemia?

The cause of WM is not known. However, hepatitis C infection appears to be a significant risk factor for the development of cryoglobulinemia (the presence of an abnormal protein in the blood that causes gelling at low temperatures), which is often associated with WM. Scientists believe genetics may play a role in WM because the disease has been seen to run in families (1).

4. What are the symptoms of Waldenström's macroglobulinemia?

Some patients do not have symptoms. For those who do have symptoms, the most common ones are weakness, severe fatigue, bleeding from the nose or gums, weight loss, and bruises or other skin lesions. Severely high levels of IgM can lead to hyperviscosity syndrome, in which the blood becomes abnormally thick. Symptoms of this syndrome include visual problems (e.g., blurring or loss of vision) and neurological problems (e.g., headache, dizziness, vertigo). During a physical exam, a doctor may also find swelling of the lymph nodes, spleen, and/or liver (2).

5. How is Waldenström's macroglobulinemia diagnosed?

Initial diagnosis of WM is based on blood test and bone marrow biopsy results. Blood tests are used to determine the level of IgM in the blood and the presence of proteins, or tumor markers, that can indicate WM. For the biopsy, a sample of bone marrow (soft, sponge-like tissue in the center of most bones) is removed, usually from the hip, through a needle for examination under a microscope. The pathologist (a doctor who identifies diseases by studying cells and tissue under a microscope) looks for certain types of lymphocytes (white blood cells) that indicate WM (1). Flow cytometry (a method of measuring cell properties using a light-sensitive dye and laser or other type of light) is often used to look at markers on the cell surface or inside the lymphocytes.

Additional tests may be recommended to confirm the diagnosis. A computed tomography (CT or CAT) scan uses a computer linked to an x-ray machine to create pictures of areas inside the body. This test may be used to evaluate the chest, abdomen, and pelvis, particularly swelling of the lymph nodes, liver, and/or spleen (1). A skeletal

survey (x-rays of the skeleton) can help distinguish between WM and a similar plasma cell cancer, multiple myeloma (1).

6. How is Waldenström's macroglobulinemia treated?

At this time, there is no known cure for WM. However, several treatment options are available to prevent or control the symptoms of the disease.

Patients who do not have symptoms of WM are usually monitored without being treated; these patients often live for many years before requiring treatment (2). Patients with symptoms are usually treated with chemotherapy. Biological therapy (treatment that stimulates the immune system to fight cancer) is also used to treat WM (3). Promising results have been seen with biological therapy and chemotherapy in combination. An example of combination therapy uses rituximab and fludarabine (4). Patients with high levels of IgM and hyperviscosity syndrome may undergo plasmapheresis. In this procedure, blood from the patient is removed and circulated through a machine that separates the plasma (which contains the antibody IgM) from other parts of the blood (red blood cells, white blood cells, and platelets). The red and white blood cells and platelets are returned to the patient, along with a plasma substitute (4). Plasmapheresis is often followed by chemotherapy.

Because WM is rare, some doctors may suggest treatments that have been effective in some cases, but are not considered standard treatment and/or are under study in clinical trials (research studies with people). Some of these treatments include (4):

- **High-dose chemotherapy with autologous stem cell transplantation**—blood-forming stem cells (cells from which all blood cells develop) are harvested (removed) and stored, then given back to the patient following high-dose chemotherapy. The harvested cells may be treated before transplantation to get rid of cancer cells. The transplanted cells travel to the bone marrow and begin to produce new blood cells.

- **Splenectomy**—surgery to remove the spleen. This procedure has been used in WM patients who have a significantly enlarged spleen. Some WM patients who have had this procedure have experienced remissions (decrease in or disappearance of signs or symptoms of cancer) lasting for many years. The remissions are believed to be due to the removal of a major source of IgM production.

- **Thalidomide and bortezomib**—drugs used to treat multiple myeloma, a disease similar to WM. Side effects of thalidomide include constipation, weakness, and peripheral neuropathy (a problem in nerve function that causes pain, numbness, tingling, swelling, and muscle weakness). Both agents are currently being studied in clinical trials for WM.

- **Oblimersen**—a substance being studied for cancer treatment that is believed to kill cancer cells by blocking the production of a protein that makes cancer cells live

longer, thus making them more sensitive to anticancer drugs. It is in early clinical trials for WM.

- **Sildenafil**—WM patients taking this drug for treatment of erectile dysfunction showed improvement in WM symptoms. Clinical trials are planned.

7. Where can people get more information about clinical trials?

Participation in clinical trials is an important treatment option for patients with WM. In addition to the trials mentioned in Question 6, the NCI is sponsoring several trials using combinations of agents and therapies.

People interested in taking part in a clinical trial should talk with their doctor. Information about clinical trials is available from the NCI's Cancer Information Service (CIS) (see below) at 1–800–4–CANCER and in the NCI booklet *Taking Part in Clinical Trials: What Cancer Patients Need To Know*, which can be found at http://www.cancer.gov/publications on the Internet. This booklet describes how research studies are carried out and explains their possible benefits and risks. Further information about clinical trials is available at http://www.cancer.gov/clinicaltrials on the NCI's Web site. The Web site offers detailed information about specific ongoing studies by linking to PDQ®, the NCI's comprehensive cancer information database. The CIS also provides information from PDQ.

Selected References

1. Munshi NC, Anderson KC. Plasma cell neoplasms. In: DeVita VT Jr., Hellman S, Rosenberg SA, editors. *Cancer: Principles and Practice of Oncology*. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2004.

2. Richardson P, Hideshima T, Anderson KC. Multiple myeloma and related disorders. In: Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, editors. *Clinical Oncology*. 3rd ed. London: Churchill Livingstone, 2004.

3. Gertz MA, Anagnostopoulos A, Anderson K, et al. Treatment recommendations in Waldenstrom's macroglobulinemia: Consensus panel recommendations from the Second International Workshop on Waldenstrom's Macroglobulinemia. *Seminars in Oncology* 2003; 30(2):121–126.

4. Dimopoulos MA, Kyle RA, Anagnostopoulos A, Treon SP. Diagnosis and management of Waldenstrom's macroglobulinemia. *Journal of Clinical Oncology* 2005; 23(7): 1564–1577.

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Related Resources

Publications (available at http://www.cancer.gov/publications)

- National Cancer Institute Fact Sheet 5.2, *Computed Tomography (CT): Questions and Answers*
- National Cancer Institute Fact Sheet 5.18, *Tumor Markers*
- National Cancer Institute Fact Sheet 7.2, *Biological Therapies for Cancer: Questions and Answers*
- National Cancer Institute Fact Sheet 7.49, *Targeted Cancer Therapies: Questions and Answers*
- *Biological Therapy: Treatments That Use Your Immune System To Fight Cancer*
- *Chemotherapy and You: A Guide to Self-Help During Cancer Treatment*
- *Taking Part in Clinical Trials: What Cancer Patients Need To Know*

National Cancer Institute (NCI) Resources

Cancer Information Service (toll-free)

Telephone: 1–800–4–CANCER (1–800–422–6237)
TTY: 1–800–332–8615

Online

NCI's Web site: http://www.cancer.gov
LiveHelp, NCI's live online assistance:
https://cissecure.nci.nih.gov/livehelp/welcome.asp

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