CONDITION

Waldenstrom macroglobulinemia

Waldenstrom macroglobulinemia is a slow-growing blood cancer that causes abnormal cells to make too much IgM antibody.

WHAT IT IS
Slow-growing blood cancer producing excess IgM antibody

BODY SYSTEM
Blood, bone marrow, lymphatic and immune systems

MAIN SYMPTOMS
Fatigue, weakness, numbness, vision changes

WHAT CAUSES IT
Acquired cell changes; exact cause unknown

HOW IT IS DIAGNOSED
Blood tests and bone marrow biopsy

MAIN TREATMENT
Monitoring, antibody-based therapy, targeted drugs, or chemotherapy

CAN IT BE CURED?
No, but treatment often controls it

IS IT AN EMERGENCY?
Sometimes, with sudden vision or neurological symptoms

LONG-TERM OUTLOOK
Often slow-growing, with repeated monitoring and treatment

Overview

Waldenstrom macroglobulinemia is a rare, usually slow-growing type of blood cancer. It begins in white blood cells called B lymphocytes, which normally help your immune system make antibodies.

The abnormal cells have features of both lymphocytes and antibody-producing plasma cells. They collect mainly in the bone marrow, the soft tissue inside bones where blood cells are made. This condition is therefore classified as a type of lymphoplasmacytic lymphoma.

The abnormal cells make too much of an antibody called immunoglobulin M, or IgM. A high IgM level can thicken the blood and affect circulation. The cells can also crowd out healthy blood-forming cells, leading to low red blood cells, low platelets, or reduced immune function.

Some people have no symptoms when the condition is found. They may not need treatment for months or years. Treatment is usually started because of symptoms or organ problems, not simply because an IgM result is high.

Waldenstrom macroglobulinemia is not currently considered curable with standard treatment. However, treatment can often reduce the abnormal cells and control symptoms for meaningful periods.

Symptoms

Symptoms can develop slowly and may have several possible causes. Having one of these symptoms does not mean that you have Waldenstrom macroglobulinemia.

Common effects include:

Excess IgM can make the blood unusually thick. This is called hyperviscosity . It may cause headaches, dizziness, blurred or double vision, confusion, unusual bleeding, or problems with balance. Severe symptoms need urgent assessment.

IgM may also react abnormally to cold or attach to nerves and tissues. This can contribute to painful fingers and toes in cold temperatures, skin color changes, joint pain, kidney problems, or peripheral neuropathy. Peripheral neuropathy means damage to nerves outside the brain and spinal cord, often causing numbness or burning in the feet.

- Tiredness, weakness, shortness of breath, or pale skin from anemia
- Numbness, burning, tingling, or pain in the feet or hands
- Enlarged lymph nodes or a feeling of fullness from an enlarged spleen
- Unexplained weight loss, fevers, or drenching night sweats
- Easy bruising, nosebleeds, or bleeding gums
- Frequent or slow-to-clear infections

Causes and risk factors

The exact cause is not known. Waldenstrom macroglobulinemia develops when a B lymphocyte acquires genetic changes that allow it to survive and multiply when it should not.

Many affected cells have a change in a gene called MYD88 . Some have changes in another gene called CXCR4 . These changes are usually acquired during life rather than inherited from a parent. Testing for them can support the diagnosis and may help guide treatment, but no

single gene test confirms the condition by itself.

Factors linked with a higher chance of developing it include:

IgM MGUS means a small amount of abnormal IgM is present without cancer-related symptoms or organ damage. Most people with IgM MGUS do not develop Waldenstrom macroglobulinemia, but regular follow-up is important.

Nothing you did caused the abnormal cells to develop.

- Older age
- Being male
- A close relative with Waldenstrom macroglobulinemia or another B-cell condition
- Having IgM monoclonal gammopathy of undetermined significance, or IgM MGUS

Diagnosis

Diagnosis usually begins with blood tests. A complete blood count checks red cells, white cells, and platelets. Other tests measure IgM and look for a single abnormal antibody, called a monoclonal protein or M protein.

Doctors may also check kidney and liver function, blood thickness, and markers of cell activity. Additional blood or urine tests may look for cold-reacting antibodies, nerve-related antibodies, or abnormal proteins affecting organs.

A bone marrow biopsy is needed to confirm the diagnosis. During this procedure, a small sample of liquid marrow and bone is usually taken from the back of the hip under local anesthetic. A laboratory examines the types and number of abnormal cells.

The marrow cells may be tested for MYD88 and CXCR4 changes. These results can help distinguish Waldenstrom macroglobulinemia from other conditions that produce IgM.

Scans are not always required, but CT or other imaging may be used to look for enlarged lymph nodes, liver, or spleen. An eye examination may be needed if there are vision symptoms or concern about hyperviscosity.

The results also help separate Waldenstrom macroglobulinemia from IgM MGUS, multiple myeloma, and other lymphomas. There is no standard numbered staging system like those used for many solid cancers. Instead, clinicians assess symptoms, blood counts, IgM-related problems, organ involvement, age, and other health conditions.

Treatment and management

If you have no related symptoms or organ damage, active monitoring may be safer than starting treatment immediately. This is sometimes called watch and wait . It does not mean that the condition is being ignored. Follow-up generally includes symptom reviews, examinations, and blood tests.

Treatment may be considered when the condition causes significant anemia, nerve damage, troublesome enlarged organs or lymph nodes, hyperviscosity, abnormal bleeding, kidney problems, or other IgM-related complications.

Treatment options include antibody therapy, targeted medicines, and chemotherapy. Rituximab is an antibody medicine that attaches to a protein on abnormal B cells. It may be combined with medicines such as bendamustine, bortezomib, or cyclophosphamide. The exact combination is chosen according to your symptoms, general health, previous treatment, and laboratory findings.

Targeted medicines called Bruton tyrosine kinase inhibitors , or BTK inhibitors, block signals that help the abnormal cells survive. These medicines are generally taken by mouth and may be continued while they are controlling the condition and side effects remain manageable.

Rituximab can temporarily raise the IgM level in some people. This is called an IgM flare . The care team plans monitoring and treatment around this risk, especially when IgM is already high.

Plasma exchange, also called plasmapheresis, may be used when hyperviscosity is causing symptoms. Blood passes through a machine that removes IgM-containing plasma and returns the blood cells with replacement fluid. This can improve symptoms quickly, but it does not stop the abnormal cells from making more IgM. Treatment aimed at those cells is usually also needed.

Stem cell transplantation is not routine first treatment. It may be considered in selected people whose condition has returned or has been difficult to control.

Complications

Possible complications come from the abnormal cells, excess IgM, or treatment.

Anemia can cause ongoing tiredness and breathlessness. Low platelets may increase bruising or bleeding. Reduced normal antibody production can make some infections more likely.

Hyperviscosity can interfere with blood flow to the eyes, brain, and other organs. Prompt treatment usually focuses on lowering blood thickness and controlling IgM production.

Other possible complications include:

Treatment can also cause infections, low blood counts, bleeding, heart rhythm problems, or other side effects. The risks differ between medicines. Monitoring is used to identify problems early and adjust care when needed.

- Peripheral neuropathy, which may persist even after IgM improves
- Cryoglobulinemia, in which proteins clump in the cold and affect circulation
- Cold agglutinin-related destruction of red blood cells
- Amyloidosis, caused by abnormal protein deposits in tissues
- Kidney, heart, or skin problems related to abnormal proteins
- Transformation into a faster-growing lymphoma, which is uncommon

Prevention

There is no known way to prevent Waldenstrom macroglobulinemia. The cell changes linked with it are usually acquired and are not caused by diet, exercise, stress, or another personal choice.

If you have IgM MGUS or a strong family history of related blood conditions, follow-up may identify changes earlier. Screening people without symptoms or a known risk factor is not routine.

Healthy habits cannot prevent this condition, but they may support your general health and your ability to manage treatment. These include staying physically active within your limits, avoiding smoking, eating a balanced diet, and keeping recommended vaccinations up to date.

Living with it and what to expect

Waldenstrom macroglobulinemia often behaves as a long-term condition. Some people remain well without treatment for years. Others need treatment soon after diagnosis because of anemia, hyperviscosity, nerve symptoms, or organ involvement.

Treatment can produce a remission, meaning symptoms improve and the amount of abnormal protein or cancer cells falls. Remission does not mean that every abnormal cell has gone. The condition commonly returns, and further treatment may be needed.

Follow-up continues even when you feel well. Blood counts, IgM, symptoms, and physical findings are considered together. An IgM change alone does not always mean that treatment is needed.

Many people continue work, travel, exercise, and family activities, although appointments and fatigue may require adjustments. Nerve symptoms can take longer to improve than blood results and may not fully reverse. Rehabilitation, pain management, and practical support may help.

The outlook is influenced by age, overall health, blood counts, the condition's biological features, complications, and response to treatment. Because newer treatment options have expanded, decisions may change over time. No individual course can be predicted from one blood result.

When to get medical help

Arrange a routine appointment if you develop persistent fatigue, new numbness or burning in your hands or feet, increasing bruising, repeated infections, swollen lymph nodes, or unexplained weight loss. If you already have the condition, report new symptoms rather than waiting for the next planned blood test.

Contact your care team promptly for worsening shortness of breath, increasing weakness, new bleeding, rapidly increasing swelling, fever during treatment, or symptoms of an infection. Follow any specific instructions you have been given for fever or low blood counts.

Seek emergency medical help for:

These symptoms can have causes other than Waldenstrom macroglobulinemia, but they require immediate assessment.

- Sudden loss or major change in vision
- New confusion, fainting, severe dizziness, or difficulty speaking
- New weakness or numbness affecting one side of the body
- A severe or rapidly worsening headache
- Chest pain or severe difficulty breathing
- Heavy bleeding that does not stop

Common questions

Is Waldenstrom macroglobulinemia leukemia or lymphoma?

It is classified as a type of non-Hodgkin lymphoma called lymphoplasmacytic lymphoma. The abnormal cells mainly collect in bone marrow and make excess IgM. It can share some features

with leukemia and plasma cell conditions, but it is managed as a distinct condition.

Do I need treatment as soon as I am diagnosed?

Not always. If you have no symptoms or organ damage, monitoring may be recommended. Starting treatment before it is needed has not been shown to benefit everyone and can expose you to unnecessary side effects. Treatment is generally based on what the condition is doing, not the IgM number alone.

Is a high IgM level always dangerous?

No. The level needs to be considered with symptoms, examination findings, blood counts, and sometimes a blood-thickness test. Some people tolerate a high level without hyperviscosity, while others develop symptoms at a lower level. Sudden vision or neurological symptoms need urgent assessment.

Can Waldenstrom macroglobulinemia run in families?

Family members may have a somewhat higher chance of this or another B-cell condition, but most relatives will not develop it. The mutations found in the cancer cells are generally acquired, not directly passed from parent to child. Routine genetic testing of relatives is not usually part of diagnosis.

What is the difference between IgM MGUS and Waldenstrom macroglobulinemia?

Both involve an abnormal IgM protein. IgM MGUS has a smaller abnormal cell population and does not cause related symptoms or organ damage. A bone marrow biopsy and other test results help distinguish them.

Can it come back after treatment?

Yes. Treatment can control the condition for long periods, but it does not usually remove every abnormal cell. If it returns, the next treatment is chosen according to your symptoms, previous response, side effects, gene-test results, and available options.

Sources

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