Waldenström macroglobulinemia

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Waldenström macroglobulinemia is a rare blood cell cancer characterized by an excess of abnormal white blood cells called lymphoplasmacytic cells in the bone marrow. This condition is classified as a lymphoplasmacytic lymphoma. The abnormal cells have characteristics of both white blood cells (lymphocytes) called B cells and of more mature cells derived from B cells known as plasma cells. These abnormal cells produce excess amounts of IgM, a type of protein known as an immunoglobulin; the overproduction of this large protein is how the condition got its name ("macroglobulinemia").

Keywords: genetic conditions

1. Introduction

Waldenström macroglobulinemia usually begins in a person's sixties and is a slow-growing (indolent) cancer. Some affected individuals have elevated levels of IgM and lymphoplasmacytic cells but no symptoms of the condition; in these cases, the disease is usually found incidentally by a blood test taken for another reason. These individuals are diagnosed with smoldering (or asymptomatic) Waldenström macroglobulinemia. It can be several years before this form of the condition progresses to the symptomatic form.

Individuals with symptomatic Waldenström macroglobulinemia can experience general symptoms such as fever, night sweats, and weight loss. Several other signs and symptoms of the condition are related to the excess IgM, which can thicken blood and impair circulation, causing a condition known as hyperviscosity syndrome. Features related to hyperviscosity syndrome include bleeding in the nose or mouth, blurring or loss of vision, headache, dizziness, and difficulty coordinating movements (ataxia). In some affected individuals, the IgM proteins clump together in the hands and feet, where the body temperature is cooler than at the center of the body. These proteins are then referred to as cryoglobulins, and their clumping causes a condition known as cryoglobulinemia. Cryoglobulinemia can lead to pain in the hands and feet or episodes of Raynaud phenomenon, in which the fingers and toes turn white or blue in response to cold temperatures. The IgM protein can also build up in organs such as the heart and kidneys, causing a condition called amyloidosis, which can lead to heart and kidney problems. Some people with Waldenström macroglobulinemia develop a loss of sensation and weakness in the limbs (peripheral neuropathy). Doctors are unsure why this feature occurs, although they speculate that the IgM protein attaches to the protective covering of nerve cells (myelin) and breaks it down. The damaged nerves cannot carry signals normally, leading to neuropathy.

Other features of Waldenström macroglobulinemia are due to the accumulation of lymphoplasmacytic cells in different tissues. For example, accumulation of these cells can lead to an enlarged liver (hepatomegaly), spleen (splenomegaly), or lymph nodes (lymphadenopathy). In the bone marrow, the lymphoplasmacytic cells interfere with normal blood cell development, causing a shortage of normal blood cells (pancytopenia). Excessive tiredness (fatigue) due to a reduction in red blood cells (anemia) is common in affected individuals.

2. Frequency

Waldenström macroglobulinemia affects an estimated 3 per million people each year in the United States. Approximately 1,500 new cases of the condition are diagnosed each year in this country, and whites are more commonly affected than African Americans. For unknown reasons, the condition occurs twice as often in men than women.

3. Causes

Waldenström macroglobulinemia is thought to result from a combination of genetic changes. The most common known genetic change associated with this condition is a mutation in the *MYD88* gene, which is found in more than 90 percent of affected individuals. Another gene commonly associated with Waldenström macroglobulinemia, *CXCR4*, is mutated in approximately 30 percent of affected individuals (most of whom also have the *MYD88* gene mutation). Other genetic changes believed to be involved in Waldenström macroglobulinemia have not yet been identified. Studies have found that certain regions of DNA are deleted or added in some people with the condition; however, researchers are unsure which genes in these regions are important for development of the condition. The mutations that cause Waldenström macroglobulinemia are acquired during a person's lifetime and are present only in the abnormal blood cells.

The proteins produced from the *MYD88* and *CXCR4* genes are both involved in signaling within cells. The MyD88 protein relays signals that help prevent the self-destruction (apoptosis) of cells, thus aiding in cell survival. The CXCR4 protein stimulates signaling pathways inside the cell that help regulate cell growth and division (proliferation) and cell survival. Mutations in these genes lead to production of proteins that are constantly functioning (overactive). Excessive signaling through these overactive proteins allows survival and proliferation of abnormal cells that should undergo apoptosis, which likely contributes to the accumulation of lymphoplasmacytic cells in Waldenström macroglobulinemia.

3.1 The genes associated with Waldenström macroglobulinemia

- CXCR4
- MYD88

4. Inheritance

Waldenström macroglobulinemia is usually not inherited, and most affected people have no history of the disorder in their family. The condition usually arises from mutations that are acquired during a person's lifetime (somatic mutations), which are not inherited.

Some families seem to have a predisposition to the condition. Approximately 20 percent of people with Waldenström macroglobulinemia have a family member with the condition or another disorder involving abnormal B cells.

5. Other Names for This Condition

- macroglobulinemia of Waldenstrom
- Waldenstrom macroglobulinemia
- Waldenstrom's macroglobulinemia
- WM

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