WAS Gene

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Wiskott-Aldrich syndrome is characterized by abnormal immune system function (immune deficiency), eczema (an inflammatory skin disorder characterized by abnormal patches of red, irritated skin), and a reduced ability to form blood clots. This condition primarily affects males.

Keywords: genetic conditions

1. Introduction

Individuals with Wiskott-Aldrich syndrome have microthrombocytopenia, which is a decrease in the number and size of blood cells involved in clotting (platelets). This platelet abnormality, which is typically present from birth, can lead to easy bruising, bloody diarrhea, or episodes of prolonged bleeding following nose bleeds or minor trauma. Microthrombocytopenia can also lead to small areas of bleeding just under the surface of the skin, resulting in purplish spots called purpura, or variably sized rashes made up of tiny red spots called petechiae. In some cases, particularly if a bleeding episode occurs within the brain, prolonged bleeding can be life-threatening.

Wiskott-Aldrich syndrome is also characterized by abnormal or nonfunctional immune system cells known as white blood cells. Changes in white blood cells lead to an increased risk of several immune and inflammatory disorders in people with Wiskott-Aldrich syndrome. These immune problems vary in severity and include an increased susceptibility to infection from bacteria, viruses, and fungi. People with Wiskott-Aldrich syndrome are at greater risk of developing autoimmune disorders, such as rheumatoid arthritis, vasculitis, or hemolytic anemia. These disorder occur when the immune system malfunctions and attacks the body's own tissues and organs. The chance of developing certain types of cancer, such as cancer of the immune system cells (lymphoma), is also increased in people with Wiskott-Aldrich syndrome.

Wiskott-Aldrich syndrome is often considered to be part of a disease spectrum with two other disorders: X-linked thrombocytopenia and severe congenital neutropenia. These conditions have overlapping signs and symptoms and the same genetic cause.

2. Normal Function

The *WAS* gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling triggers the cell to move and attach to other cells and tissues (adhesion). In white blood cells, which protect the body from infection, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

3. Health Conditions Related to Genetic Changes

3.1 Wiskott-Aldrich syndrome

More than 350 mutations in the *WAS* gene have been found to cause Wiskott-Aldrich syndrome, a condition characterized by abnormal immune system function (immune deficiency) and a reduced ability to form blood clots leading to prolonged bleeding episodes. Most of the mutations lead to the production of an abnormally short, nonfunctional version of WASP or prevent the production of any WASP. As a result, WASP cannot relay signals, which disrupts the function of the actin cytoskeleton in developing blood cells. White blood cells that lack WASP have a decreased ability to respond to their environment and form immune synapses. As a result, white blood cells are less able to respond to foreign invaders, causing many of the immune problems related to Wiskott-Aldrich syndrome. Similarly, when cells that aid blood clot

formation (platelets) lack functional WASP, their development is impaired. A reduction in platelet size and early cell death leads to the bleeding problems in affected individuals. The impairments of white blood cells and platelets are largely responsible for the immune deficiency and bleeding problems characteristic of Wiskott-Aldrich syndrome.

3.2 X-linked thrombocytopenia

More than 60 mutations in the *WAS* gene have been found to cause X-linked thrombocytopenia, a blood disorder characterized by a decrease in the amount and size of platelets, leading to prolonged bleeding episodes. Immune problems such as an increased susceptibility to infections may also occur. Most of these *WAS* gene mutations change single protein building blocks (amino acids) in WASP. Mutations typically lead to the production of an altered protein that cannot efficiently relay signals from the cell membrane to the actin cytoskeleton. In people with X-linked thrombocytopenia, these signaling problems primarily affect the development of platelets. In some cases, white blood cells are affected. When WASP function is impaired in white blood cells, these cells are less able to respond to foreign invaders and immune disorders are more likely to occur.

Some *WAS* gene mutations cause X-linked thrombocytopenia in some individuals and a related condition called Wiskott-Aldrich syndrome (described above) in others. These mutations usually prevent the production of any WASP. It is unknown why some people with these mutations have the relatively mild features of X-linked thrombocytopenia and others have the severe symptoms of Wiskott-Aldrich syndrome. Because they have overlapping features and the same genetic cause, Wiskott-Aldrich syndrome, X-linked thrombocytopenia, and severe congenital neutropenia are sometimes collectively referred to as WAS-related disorders.

4. Other Names for This Gene

- IMD2
- WASP
- WASP_HUMAN
- WASPA
- Wiskott-Aldrich syndrome (eczema-thrombocytopenia)
- Wiskott-Aldrich syndrome protein

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