Langerhans Cell Histiocytosis

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Langerhans cell histiocytosis is a disorder in which excess immune system cells called Langerhans cells build up in the body.

genetic conditions

1. Introduction

Langerhans cells, which help regulate the immune system, are normally found throughout the body, especially in the skin, lymph nodes, spleen, lungs, liver, and bone marrow. In Langerhans cell histiocytosis, excess immature Langerhans cells usually form tumors called granulomas. Many researchers now consider Langerhans cell histiocytosis to be a form of cancer, but this classification remains controversial.

In approximately 80 percent of affected individuals, one or more granulomas develop in the bones, causing pain and swelling. The granulomas, which usually occur in the skull or the long bones of the arms or legs, may cause the bone to fracture.

Granulomas also frequently occur in the skin, appearing as blisters, reddish bumps, or rashes which can be mild to severe. The pituitary gland may also be affected; this gland is located at the base of the brain and produces hormones that control many important body functions. Without hormone supplementation, affected individuals may experience delayed or absent puberty or an inability to have children (infertility). In addition, pituitary gland damage may result in the production of excessive amounts of urine (diabetes insipidus) and dysfunction of another gland called the thyroid. Thyroid dysfunction can affect the rate of chemical reactions in the body (metabolism), body temperature, skin and hair texture, and behavior.

In 15 to 20 percent of cases, Langerhans cell histiocytosis affects the lungs, liver, or blood-forming (hematopoietic) system; damage to these organs and tissues may be life-threatening. Lung involvement, which appears as swelling of the small airways (bronchioles) and blood vessels of the lungs, results in stiffening of the lung tissue, breathing problems, and increased risk of infection. Hematopoietic involvement, which occurs when the Langerhans cells crowd out blood-forming cells in the bone marrow, leads to a general reduction in the number of blood cells (pancytopenia). Pancytopenia results in fatigue due to low numbers of red blood cells (anemia), frequent infections due to low numbers of white blood cells (neutropenia), and clotting problems due to low numbers of platelets (thrombocytopenia).

Other signs and symptoms that may occur in Langerhans cell histiocytosis, depending on which organs and tissues have Langerhans cell deposits, include swollen lymph nodes, abdominal pain, yellowing of the skin and whites of the eyes (jaundice), delayed puberty, protruding eyes, dizziness, irritability, and seizures. About 1 in 50 affected individuals experience deterioration of neurological function (neurodegeneration).

Langerhans cell histiocytosis is often diagnosed in childhood, usually between ages 2 and 3, but can appear at any age. Most individuals with adult-onset Langerhans cell histiocytosis are current or past smokers; in about two-thirds of adult-onset cases the disorder affects only the lungs.

The severity of Langerhans cell histiocytosis, and its signs and symptoms, vary widely among affected individuals. Certain presentations or forms of the disorder were formerly considered to be separate diseases. Older names that were sometimes used for forms of Langerhans cell histiocytosis include eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease.

In many people with Langerhans cell histiocytosis, the disorder eventually goes away with appropriate treatment. It may even disappear on its own, especially if the disease occurs only in the skin. However, some complications of the condition, such as diabetes insipidus or other effects of tissue and organ damage, may be permanent.

2. Frequency

Langerhans cell histiocytosis is a rare disorder. Its prevalence is estimated at 1 to 2 in 100,000 people.

3. Causes

Somatic mutations in the *BRAF* gene have been identified in the Langerhans cells of about half of individuals with Langerhans cell histiocytosis. Somatic gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes are not inherited.

The *BRAF* gene provides instructions for making a protein that is normally switched on and off in response to signals that control cell growth and development. Somatic mutations cause the BRAF protein in affected cells to be continuously active and to transmit messages to the nucleus even in the absence of these chemical signals. The overactive protein may contribute to the development of Langerhans cell histiocytosis by allowing the Langerhans cells to grow and divide uncontrollably.

Changes in other genes have also been identified in the Langerhans cells of some individuals with Langerhans cell histiocytosis. Some researchers believe that additional factors, such as viral infections and environmental toxins, may also influence the development of this complex disorder.

3.1. The genes associated with Langerhans cell histiocytosis

- BRAF
- MAP2K1
- MAP3K1

4. Inheritance

Langerhans cell histiocytosis is usually not inherited and typically occurs in people with no history of the disorder in their family.

A few families with multiple cases of Langerhans cell histiocytosis have been identified, but the inheritance pattern is unknown.

5. Other Names for This Condition

- Hashimoto-Pritzger disease
- histiocytosis X
- Langerhans cell granulomatosis
- LCH

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