Erdheim-Chester Disease

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Contributor: Nicole Yin

Erdheim-Chester disease is a rare type of slow-growing blood cancer called a histiocytic neoplasm, which results in overproduction of cells called histiocytes. Histiocytes normally function to destroy foreign substances and protect the body from infection. In Erdheim-Chester disease, the excess production of histiocytes (histiocytosis) leads to inflammation that can damage organs and tissues throughout the body, causing them to become thickened, dense, and scarred (fibrotic); this tissue damage may lead to organ failure.

genetic conditions

1. Introduction

People with Erdheim-Chester disease often have bone pain, especially in the lower legs and upper arms, due to an abnormal increase in bone density (osteosclerosis). Damage to the pituitary gland (a structure at the base of the brain that produces several hormones, including a hormone that controls the amount of water released in the urine) may result in hormonal problems such as a condition called diabetes insipidus that leads to excessive urination. Abnormally high pressure of the cerebrospinal fluid within the skull (intracranial hypertension) caused by accumulation of histiocytes in the brain may result in headaches, seizures, cognitive impairment, or problems with movement or sensation. People with this condition can also have shortness of breath, heart or kidney disease, protruding eyes (exophthalmos), skin growths, or inability to conceive a child (infertility). Affected individuals may also experience fever, night sweats, fatigue, weakness, and weight loss.

The signs and symptoms of Erdheim-Chester disease usually appear between the ages of 40 and 60, although the disorder can occur at any age. The severity of the condition varies widely; some affected individuals have few or no associated health problems, while others have severe complications that can be life-threatening.

2. Frequency

Erdheim-Chester disease is a rare disorder; its exact prevalence is unknown. More than 500 affected individuals worldwide have been described in the medical literature. For unknown reasons, men are slightly more likely to develop the disease, accounting for about 60 percent of cases.

3. Causes

More than half of people with Erdheim-Chester disease have a specific mutation in the *BRAF* gene. Mutations in other genes are also thought to be involved in this disorder.

The *BRAF* gene provides instructions for making a protein that helps transmit chemical signals from outside the cell to the cell's nucleus. This protein is part of a signaling pathway known as the RAS/MAPK pathway, which controls several important cell functions. Specifically, the RAS/MAPK pathway regulates the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), cell movement (migration), and the self-destruction of cells (apoptosis).

The *BRAF* gene mutation that causes Erdheim-Chester disease is somatic, which means that it occurs during a person's lifetime and is present only in certain cells. The mutation occurs in histiocytes or in immature precursor cells that will develop into histiocytes. This mutation leads to production of a BRAF protein that is abnormally active, which disrupts regulation of cell growth and division. The unregulated overproduction of histiocytes results in their accumulation in the body's tissues and organs, leading to the signs and symptoms of Erdheim-Chester disease.

3.1. The Gene Associated with Erdheim-Chester Disease

- BRAF

4. Inheritance

This condition is not inherited. It arises from a somatic mutation in histiocytes or their precursor cells during an individual's lifetime.

5. Other Names for This Condition

- lipid granulomatosis
- polyostotic sclerosing histiocytosis

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