PDGFRA-Associated Chronic Eosinophilic Leukemia

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Contributor: Rita Xu

PDGFRA-associated chronic eosinophilic leukemia is a form of blood cell cancer characterized by an elevated number of cells called eosinophils in the blood. These cells help fight infections by certain parasites and are involved in the inflammation associated with allergic reactions. However, these circumstances do not account for the increased number of eosinophils in *PDGFRA*-associated chronic eosinophilic leukemia.

Keywords: genetic conditions

1. Introduction

Another characteristic feature of *PDGFRA*-associated chronic eosinophilic leukemia is organ damage caused by the excess eosinophils. Eosinophils release substances to aid in the immune response, but the release of excessive amounts of these substances causes damage to one or more organs, most commonly the heart, skin, lungs, or nervous system. Eosinophil-associated organ damage can lead to a heart condition known as eosinophilic endomyocardial disease, skin rashes, coughing, difficulty breathing, swelling (edema) in the lower limbs, confusion, changes in behavior, or impaired movement or sensations. People with *PDGFRA*-associated chronic eosinophilic leukemia can also have an enlarged spleen (splenomegaly) and elevated levels of certain chemicals called vitamin B12 and tryptase in the blood.

Some people with *PDGFRA*-associated chronic eosinophilic leukemia have an increased number of other types of white blood cells, such as neutrophils or mast cells. Occasionally, people with *PDGFRA*-associated chronic eosinophilic leukemia develop other blood cell cancers, such as acute myeloid leukemia or B-cell or T-cell acute lymphoblastic leukemia or lymphoblastic lymphoma.

PDGFRA-associated chronic eosinophilic leukemia is often grouped with a related condition called hypereosinophilic syndrome. These two conditions have very similar signs and symptoms; however, the cause of hypereosinophilic syndrome is unknown.

2. Frequency

PDGFRA-associated chronic eosinophilic leukemia is a rare condition; however, the exact prevalence is unknown.

3. Causes

PDGFRA-associated chronic eosinophilic leukemia is caused by mutations in the *PDGFRA* gene. This condition usually occurs as a result of genetic rearrangements that fuse part of the *PDGFRA* gene with part of another gene. Rarely, changes in single DNA building blocks (point mutations) in the *PDGFRA* gene are found in people with this condition. Genetic rearrangements and point mutations affecting the *PDGFRA* gene are somatic mutations, which are mutations acquired during a person's lifetime that are present only in certain cells. The somatic mutation occurs initially in a single cell, which continues to grow and divide, producing a group of cells with the same mutation (a clonal population).

The most common genetic abnormality in *PDGFRA*-associated chronic eosinophilic leukemia results from a deletion of genetic material from chromosome 4, which brings together part of the *PDGFRA* gene and part of the *FIP1L1* gene, creating the *FIP1L1-PDGFRA* fusion gene.

The *FIP1L1* gene provides instructions for a protein that plays a role in forming the genetic blueprints for making proteins (messenger RNA or mRNA).

The *PDGFRA* gene provides instructions for making a receptor protein that is found in the cell membrane of certain cell types. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. When the ligand attaches (binds), the PDGFRA receptor protein is turned on (activated), which leads to activation of a series of

proteins in multiple signaling pathways. These signaling pathways control many important cellular processes, such as cell growth and division (proliferation) and cell survival.

The *FIP1L1-PDGFRA* fusion gene (as well as other *PDGFRA* fusion genes) provides instructions for making a fusion protein that has the function of the normal PDGFRA protein. However, the fusion protein does not require ligand binding to be activated. Similarly, point mutations in the *PDGFRA* gene can result in a PDGFRA protein that is activated without ligand binding. As a result, the signaling pathways are constantly turned on (constitutively activated), which increases the proliferation and survival of cells. When the *FIP1L1-PDGFRA* fusion gene mutation or point mutations in the *PDGFRA* gene occur in blood cell precursors, the growth of eosinophils (and occasionally other blood cells, such as neutrophils and mast cells) is poorly controlled, leading to *PDGFRA*-associated chronic eosinophilic leukemia. It is unclear why eosinophils are preferentially affected by this genetic change.

The Genes and Chromosome Associated with PDGFRA-Associated Chronic Eosinophilic Leukemia

- FIP1L1
- PDGFRA
- chromosome 4

4. Inheritance

PDGFRA-associated chronic eosinophilic leukemia is not inherited and occurs in people with no history of the condition in their families. Mutations that lead to a *PDGFRA* fusion gene and *PDGFRA* point mutations are somatic mutations, which means they occur during a person's lifetime and are found only in certain cells. Somatic mutations are not inherited. Males are more likely to develop *PDGFRA*-associated chronic eosinophilic leukemia than females because, for unknown reasons, *PDGFRA* fusion genes are found more often in males.

5. Other Names for This Condition

- PDGFRA-associated myeloproliferative neoplasm

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