PDGFRB-associated chronic eosinophilic leukemia

Description

PDGFRB-associated chronic eosinophilic leukemia is a type of cancer of blood-forming cells. It is characterized by an elevated number of white blood 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 *PDGFRB*-associated chronic eosinophilic leukemia. Some people with this condition have an increased number of other types of white blood cells, such as neutrophils or mast cells, in addition to eosinophils. People with this condition can have an enlarged spleen (splenomegaly) or enlarged liver (hepatomegaly). Some affected individuals develop skin rashes, likely as a result of an abnormal immune response due to the increased number of eosinophils.

Frequency

The exact prevalence of *PDGFRB*-associated chronic eosinophilic leukemia is unknown. For unknown reasons, males are up to nine times more likely than females to develop *PDGFRB*-associated chronic eosinophilic leukemia.

Causes

PDGFRB-associated chronic eosinophilic leukemia is caused by genetic rearrangements that join part of the *PDGFRB* gene with part of another gene. At least 20 genes have been found that fuse with the *PDGFRB* gene to cause *PDGFRB*-associated chronic eosinophilic leukemia. The most common genetic abnormality in this condition results from a rearrangement (translocation) of genetic material that brings part of the *PDGFRB* gene on chromosome 5 together with part of the *ETV6* gene on chromosome 12, creating the *ETV6-PDGFRB* fusion gene.

The *PDGFRB* gene provides instructions for making a protein that plays a role in turning on (activating) signaling pathways that control many cell processes, including cell growth and division (proliferation). The *ETV6* gene provides instructions for making a protein that turns off (represses) gene activity. This protein is important in development before birth and in regulating blood cell formation. The protein produced from the *ETV6-PDGFRB* fusion gene, called ETV6/PDGFRβ, functions differently than the proteins normally produced from the individual genes. Like the normal PDGFRβ protein, the ETV6/PDGFRβ fusion protein turns on signaling pathways. However, the fusion protein

does not need to be turned on to be active, so the signaling pathways are constantly turned on (constitutively activated). The fusion protein is unable to repress gene activity regulated by the normal ETV6 protein, so gene activity is increased. The constitutively active signaling pathways and abnormal gene activity increase the proliferation and survival of cells.

When the *ETV6-PDGFRB* fusion gene variant (also known as a mutation) occurs in cells that develop into blood cells, the growth of eosinophils (and occasionally other blood cells, such as neutrophils and mast cells) is poorly controlled, leading to *PDGFRB*-associated chronic eosinophilic leukemia. It is unclear why eosinophils are preferentially affected by this genetic change.

Learn more about the genes and chromosomes associated with PDGFRB-associated chronic eosinophilic leukemia

- ETV6
- PDGFRB
- chromosome 12
- chromosome 5

Inheritance

PDGFRB-associated chronic eosinophilic leukemia is not inherited and occurs in people with no history of the condition in their families. Chromosomal rearrangements that lead to a *PDGFRB* fusion gene are somatic variants, which are variants acquired during a person's lifetime and present only in certain cells. The somatic variant occurs initially in a single cell, which continues to grow and divide, producing a group of cells with the same variant (a clonal population).

Other Names for This Condition

- Chronic myelomonocytic leukemia with eosinophilia associated with t(5;12)
- Myeloid neoplasms associated with PDGFRB rearrangement
- Myeloid neoplasms with PDGFRB rearrangement
- Myeloid/lymphoid neoplasms with PDGFRB rearrangement

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Myeloproliferative disorder, chronic, with eosinophilia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1851585/)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- MYELOPROLIFERATIVE DISORDER, CHRONIC, WITH EOSINOPHILIA (https://omim.org/entry/131440)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28pdgfrb%5BTIAB%5D%29+AND+%28eosinophilia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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