Familial acute myeloid leukemia with mutated CEBPA

Familial acute myeloid leukemia with mutated *CEBPA* is one form of a cancer of the blood-forming tissue (bone marrow) called acute myeloid leukemia. In normal bone marrow, early blood cells called hematopoietic stem cells develop into several types of blood cells: white blood cells (leukocytes) that protect the body from infection; red blood cells (erythrocytes) that carry oxygen; and platelets (thrombocytes), which are involved in blood clotting. In acute myeloid leukemia, the bone marrow makes large numbers of abnormal, immature white blood cells called myeloid blasts. Instead of developing into normal white blood cells, the myeloid blasts develop into cancerous leukemia cells. The large number of abnormal cells in the bone marrow interferes with the production of functional white blood cells, red blood cells, and platelets.

People with familial acute myeloid leukemia with mutated *CEBPA* have a shortage of white blood cells (leukopenia), leading to increased susceptibility to infections. A low number of red blood cells (anemia) also occurs in this disorder, resulting in fatigue and weakness. Affected individuals also have a reduction in the amount of platelets (thrombocytopenia), which can result in easy bruising and abnormal bleeding. Other symptoms of familial acute myeloid leukemia with mutated *CEBPA* may include fever and weight loss.

While acute myeloid leukemia is generally a disease of older adults, familial acute myeloid leukemia with mutated *CEBPA* often begins earlier in life, and it has been reported to occur as early as age 4. Between 50 and 65 percent of affected individuals survive their disease, compared with 25 to 40 percent of those with other forms of acute myeloid leukemia. However, people with familial acute myeloid leukemia with mutated *CEBPA* have a higher risk of having a new primary occurrence of this disorder after successful treatment of the initial occurrence.

**Frequency**

Acute myeloid leukemia occurs in approximately 3.5 in 100,000 individuals per year. Familial acute myeloid leukemia with mutated *CEBPA* is a very rare form of acute myeloid leukemia; only a few affected families have been identified.

**Causes**

As its name suggests, familial acute myeloid leukemia with mutated *CEBPA* is caused by mutations in the *CEBPA* gene that are passed down within families. These inherited mutations are present throughout a person's life in virtually every cell in the body.

The *CEBPA* gene provides instructions for making a protein called CCAAT enhancer-binding protein alpha. This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. It
is believed to act as a tumor suppressor, helping to prevent cells from growing and dividing too rapidly or in an uncontrolled way.

*CEBPA* gene mutations that cause familial acute myeloid leukemia with mutated *CEBPA* result in a shorter version of CCAAT enhancer-binding protein alpha. This shorter version is produced from one copy of the *CEBPA* gene in each cell, and it is believed to interfere with the tumor suppressor function of the normal protein produced from the second copy of the gene. Absence of the tumor suppressor function of CCAAT enhancer-binding protein alpha is believed to disrupt the regulation of blood cell production in the bone marrow, leading to the uncontrolled production of abnormal cells that occurs in acute myeloid leukemia.

In addition to the inherited mutation in one copy of the *CEBPA* gene in each cell, most individuals with familial acute myeloid leukemia with mutated *CEBPA* also acquire a mutation in the second copy of the *CEBPA* gene. The additional mutation, which is called a somatic mutation, is found only in the leukemia cells and is not inherited. The somatic *CEBPA* gene mutations identified in leukemia cells generally decrease the DNA-binding ability of CCAAT enhancer-binding protein alpha. The effect of this second mutation on the development of acute myeloid leukemia is unclear.

**Inheritance Pattern**

Familial acute myeloid leukemia with mutated *CEBPA* is inherited in an autosomal dominant pattern. Autosomal dominant inheritance means that one copy of the altered *CEBPA* gene in each cell is sufficient to cause the disorder. Most affected individuals also acquire a second, somatic *CEBPA* gene mutation in their leukemia cells.

**Other Names for This Condition**

- CEBPA-dependent familial acute myeloid leukemia
- familial acute myeloid leukaemia

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Acute myeloid leukemia

**Research Studies from ClinicalTrials.gov**

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22familial+acute+myeloid+leukemia+with+mutated+CEBPA%22+OR+%22Leukemia%2C+Myeloid%2C+Acute%22
Other Diagnosis and Management Resources

- Fred Hutchison Cancer Research Center

- GeneReview: CEBPA-Associated Familial Acute Myeloid Leukemia (AML)
  https://www.ncbi.nlm.nih.gov/books/NBK47457

- MedlinePlus Encyclopedia: Bone Marrow Biopsy
  https://medlineplus.gov/ency/article/003934.htm

- MedlinePlus Encyclopedia: Bone Marrow Transplant
  https://medlineplus.gov/ency/article/003009.htm

- National Cancer Institute: Acute Myeloid Leukemia Treatment

- St. Jude Children's Research Hospital
  https://www.stjude.org/disease/acute-myeloid-leukemia.html?vgnextoid=775c061585f70110VgnVCM1000001e0215acRCRD

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Acute Myeloid Leukemia
  https://medlineplus.gov/ency/article/000542.htm

- Encyclopedia: Bone Marrow Biopsy
  https://medlineplus.gov/ency/article/003934.htm

- Encyclopedia: Bone Marrow Transplant
  https://medlineplus.gov/ency/article/003009.htm

- Health Topic: Acute Myeloid Leukemia
  https://medlineplus.gov/acutemyeloidleukemia.html

Additional NIH Resources

- National Cancer Institute: Acute Myeloid Leukemia Treatment

Educational Resources

- Journal of the American Medical Association: Acute Myeloid Leukemia Patient Page
  https://jamanetwork.com/journals/jama/fullarticle/184065

- MalaCards: familial acute myeloid leukemia with mutated cebpa
  https://www.malacards.org/card/familial_acute_myeloid_leukemia_with_mutated_cebpa

- Orphanet: Acute myeloid leukemia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=519
Patient Support and Advocacy Resources

- American Cancer Society
- CureSearch for Children's Cancer
  https://curesearch.org/Acute-Myeloid-Leukemia-in-Children
- The Leukemia & Lymphoma Society
  https://www.lls.org/leukemia/acute-myeloid-leukemia

Clinical Information from GeneReviews

- CEBPA-Associated Familial Acute Myeloid Leukemia (AML)
  https://www.ncbi.nlm.nih.gov/books/NBK47457

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28acute+myeloid+leukemia%5BTIAB%5D%29+AND+%28CEBPA%5BTIAB%5D%29%29+AND+english%5BBl%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- LEUKEMIA, ACUTE MYELOID
  http://omim.org/entry/601626

Sources for This Summary


Reprinted from Genetics Home Reference:

Reviewed: July 2015
Published: April 28, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services