Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy

Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy, commonly known as CARASIL, is an inherited condition that causes stroke and other impairments.

Abnormalities affecting the brain and other parts of the nervous system become apparent in an affected person's twenties or thirties. Often, muscle stiffness (spasticity) in the legs and problems with walking are the first signs of the disorder. About half of affected individuals have a stroke or similar episode before age 40. As the disease progresses, most people with CARASIL also develop mood and personality changes, a decline in thinking ability (dementia), memory loss, and worsening problems with movement.

Other characteristic features of CARASIL include premature hair loss (alopecia) and attacks of low back pain. The hair loss often begins during adolescence and is limited to the scalp. Back pain, which develops in early to mid-adulthood, results from the breakdown (degeneration) of the discs that separate the bones of the spine (vertebrae) from one another.

The signs and symptoms of CARASIL worsen slowly with time. Over the course of several years, affected individuals become less able to control their emotions and communicate with others. They increasingly require help with personal care and other activities of daily living; after a few years, they become unable to care for themselves. Most affected individuals die within a decade after signs and symptoms first appear, although few people with the disease have survived for 20 to 30 years.

Frequency

CARASIL appears to be a rare condition. It has been identified in about 50 people, primarily in Japan and China.

Causes

CARASIL is caused by mutations in the *HTRA1* gene. This gene provides instructions for making an enzyme that is found in many of the body's organs and tissues. One of the major functions of the HTRA1 enzyme is to regulate signaling by proteins in the transforming growth factor-beta (TGF-β) family. TGF-β signaling is essential for many critical cell functions. It also plays an important role in the formation of new blood vessels (angiogenesis).

In people with CARASIL, mutations in the *HTRA1* gene prevent the effective regulation of TGF-β signaling. Researchers suspect that abnormally increased TGF-β signaling alters the structure of small blood vessels, particularly in the brain. These blood vessel abnormalities (described as arteriopathy) greatly increase the risk of stroke and lead to the death of nerve cells (neurons) in many areas of the brain. Dysregulation of TGF-β signaling may also underlie the hair loss and back pain seen in people with CARASIL, although the relationship between abnormal TGF-β signaling and these features is less clear.

Inheritance Pattern

As its name suggests, this condition is inherited in an autosomal recessive pattern. Autosomal recessive inheritance means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- CARASIL
- familial young-adult-onset arteriosclerotic leukoencephalopathy with alopecia and lumbago without arterial hypertension
- Maeda syndrome
- Nemoto disease

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
- Genetic Testing Registry: Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy https://www.ncbi.nlm.nih.gov/gtr/conditions/C1838577/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22cerebral+autosomal+recessive+arteriopathy+with+subcortical+infarcts+and+leukoencephalopathy%22+OR+%22Cerebral+Arterial+Diseases%22

Other Diagnosis and Management Resources

- GeneReview: CARASIL https://www.ncbi.nlm.nih.gov/books/NBK32533

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Dementia
  https://medlineplus.gov/ency/article/000739.htm
- Encyclopedia: Low Back Pain - Acute
  https://medlineplus.gov/ency/article/007425.htm
- Encyclopedia: Stroke
  https://medlineplus.gov/ency/article/000726.htm
- Health Topic: Dementia
  https://medlineplus.gov/dementia.html
- Health Topic: Ischemic Stroke
  https://medlineplus.gov/ischemicstroke.html

Genetic and Rare Diseases Information Center

- Cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy
  https://rarediseases.info.nih.gov/diseases/10424/cerebral-autosomal-recessive-arteriopathy-with-subcortical-infarcts-and-leukoencephalopathy

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Stroke: Hope Through Research
  https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Stroke-Hope-Through-Research

Educational Resources

- MalaCards: cerebral arteriopathy, autosomal recessive, with subcortical infarcts and leukoencephalopathy
  https://www.malacards.org/card/cerebral_arteriopathy_autosomal_recessive_with_subcortical_infarcts_and_leukoencephalopathy
- Merck Manual Consumer Version: Overview of Delirium and Dementia
  https://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/delirium-and-dementia/overview-of-delirium-and-dementia
- Merck Manual Consumer Version: Overview of Stroke
  https://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/stroke-cva/overview-of-stroke
- Orphanet: CARASIL
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=199354

Patient Support and Advocacy Resources

- American Stroke Association
  https://www.strokeassociation.org/
- Family Caregiver Alliance
  https://www.caregiver.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/carasil/

Clinical Information from GeneReviews

- CARASIL
  https://www.ncbi.nlm.nih.gov/books/NBK32533

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28carasil%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- CEREBRAL ARTERIOPATHY, AUTOSOMAL RECESSIVE, WITH SUBCORTICAL INFARCTS AND LEUKOENCEPHALOPATHY
  http://omim.org/entry/600142

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