Familial cold autoinflammatory syndrome

Description

Familial cold autoinflammatory syndrome is a condition that causes episodes of fever, skin rash, and joint pain after exposure to cold temperatures. These episodes usually begin in infancy and occur throughout life.

People with this condition usually experience symptoms after cold exposure of an hour or more, although in some individuals only a few minutes of exposure is required. Symptoms may be delayed for up to a few hours after the cold exposure. Episodes last an average of 12 hours, but may continue for up to 3 days.

In people with familial cold autoinflammatory syndrome, the most common symptom that occurs during an episode is an itchy or burning rash. The rash usually begins on the face or extremities and spreads to the rest of the body. Occasionally swelling in the extremities may occur.

In addition to the skin rash, episodes are characterized by fever, chills, and joint pain, most often affecting the hands, knees, and ankles. Redness in the whites of the eye (conjunctivitis), sweating, drowsiness, headache, thirst, and nausea may also occur during an episode of this disorder.

Frequency

Familial cold autoinflammatory syndrome is a very rare condition, believed to have a prevalence of less than 1 per million people.

Causes

Mutations in the *NLRP3* and *NLRP12* genes cause familial cold autoinflammatory syndrome. The *NLRP3* gene (also known as *CIAS1*) provides instructions for making a protein called cryopyrin, and the *NLRP12* gene provides instructions for making the protein monarch-1.

Cryopyrin and monarch-1 belong to a family of proteins called nucleotide-binding domain and leucine-rich repeat containing (NLR) proteins. These proteins are involved in the immune system, helping to regulate the process of inflammation. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight microbial invaders and facilitate tissue repair. When this

has been accomplished, the body stops (inhibits) the inflammatory response to prevent damage to its own cells and tissues.

Cryopyrin is involved in the assembly of a molecular complex called an inflammasome, which helps start the inflammatory process. Mutations in the *NLRP3* gene result in a hyperactive cryopyrin protein that inappropriately triggers an inflammatory response.

Monarch-1 is involved in the inhibition of the inflammatory response. Mutations in the *NLRP12* gene appear to reduce the ability of the monarch-1 protein to inhibit inflammation.

Impairment of the body's mechanisms for controlling inflammation results in the episodes of skin rash, fever, and joint pain seen in familial cold autoinflammatory syndrome. It is unclear why episodes are triggered by cold exposure in this disorder.

Learn more about the genes associated with Familial cold autoinflammatory syndrome

- NLRP12
- NLRP3

Inheritance

This condition is inherited in an autosomal dominant pattern from an affected parent; one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Cold hypersensitivity
- Familial cold urticaria
- Familial cold-induced autoinflammatory syndrome
- FCAS
- FCU

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Familial cold autoinflammatory syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0343068/)
- Genetic Testing Registry: Familial cold autoinflammatory syndrome 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2673198/)

Genetic and Rare Diseases Information Center

- Familial cold autoinflammatory syndrome (https://rarediseases.info.nih.gov/diseases/9535/familial-cold-autoinflammatory-syndrome)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22familial+cold+autoinflammatory+syndrome%22+OR+%22Familial+Cold+Autoinflammatory+Syndrome%22)

Catalog of Genes and Diseases from OMIM

- FAMILIAL COLD AUTOINFLAMMATORY SYNDROME 1 (https://omim.org/entry/120100)
- FAMILIAL COLD AUTOINFLAMMATORY SYNDROME 2 (https://omim.org/entry/611762)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28familial+cold+autoinflammatory+syndrome%5BTIAB%5D%29+OR+%28familial+cold+urticaria%5BTIAB%5D%29+OR+%28cold+hypersensitivity%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

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