Cryopyrin-associated periodic syndromes

Description

Cryopyrin-associated periodic syndromes (CAPS) are a group of conditions that have overlapping signs and symptoms and the same genetic cause. The group includes three conditions known as familial cold autoinflammatory syndrome type 1 (FCAS1), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disorder (NOMID). These conditions were once thought to be distinct disorders but are now considered to be part of the same condition spectrum. FCAS1 is the least severe form of CAPS, MWS is intermediate in severity, and NOMID is the most severe form.

The signs and symptoms of CAPS affect multiple body systems. Generally, CAPS are characterized by periodic episodes of skin rash, fever, and joint pain. These episodes can be triggered by exposure to cold temperatures, fatigue, other stressors, or they may arise spontaneously. Episodes can last from a few hours to several days. These episodes typically begin in infancy or early childhood and persist throughout life.

While the CAPS spectrum shares similar signs and symptoms, the individual conditions tend to have distinct patterns of features. People with FCAS1 are particularly sensitive to the cold, and exposure to cold temperatures can trigger a painful or burning rash. The rash usually affects the torso and limbs but may spread to the rest of the body. In addition to fever and joint pain, other possible symptoms include muscle aches, chills, drowsiness, eye redness, headache, and nausea.

Individuals with MWS develop the typical periodic episodes of skin rash, fever, and joint pain after cold exposure, although episodes may occur spontaneously or all the time. Additionally, they can develop progressive hearing loss in their teenage years. Other features of MWS include skin lesions or kidney damage from abnormal deposits of a protein called amyloid (amyloidosis).

In people with NOMID, the signs and symptoms of the condition are usually present from birth and persists throughout life. In addition to skin rash and fever, affected individuals may have joint inflammation, swelling, and joint deformities called contractures that may restrict movement. People with NOMID typically have headaches, seizures, and cognitive impairment resulting from chronic meningitis, which is inflammation of the tissue that covers and protects the brain and spinal cord (meninges). Other features of NOMID include eye problems, short stature, distinctive facial features, and kidney damage caused by amyloidosis.

Frequency

CAPS are rare, with an estimated prevalence of 2 to 5 per million individuals, collectively. However, it is thought that the conditions are underdiagnosed since the features of CAPS are similar to other more common conditions.

Causes

CAPS are caused by variants (also known as mutations) in the *NLRP3* gene. The *NLRP3* gene provides instructions for making a protein called cryopyrin. Cryopyrin is a member of a family of proteins called intracellular "NOD-like" receptor (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 foreign invaders and help repair damaged tissues. After 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 trigger the inflammatory process.

Researchers believe that *NLRP3* gene variants that cause CAPS result in an overactive cryopyrin protein, which leads to inappropriate inflammatory responses. Impairment of the body's mechanisms for controlling inflammation results in the episodes of fever and damage to the body's cells and tissues seen in CAPS.

Learn more about the gene associated with Cryopyrin-associated periodic syndromes

- NLRP3

Inheritance

CAPS are usually inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. People with the condition are born with one altered copy of the *NLRP3* gene in each cell. In most cases, the altered gene is inherited from an affected parent. The remaining cases are a result of new variants in the *NLRP3* gene and occur in people with no history of the disorder in their family.

Rarely, the genetic change that causes CAPS is not inherited but occurs at some point during embryonic development or later in life. As cells continue to grow and divide, some of these cells will have the genetic change, and others will not (a situation known as mosaicism).

Other Names for This Condition

- CAPS
- Cryopyrinopathy
- NLRP3-associated autoinflammatory disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Chronic infantile neurological, cutaneous and articular syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0409818/)
- Genetic Testing Registry: Familial amyloid nephropathy with urticaria AND deafness (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268390/)
- Genetic Testing Registry: Familial cold autoinflammatory syndrome 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4551895/)

Genetic and Rare Diseases Information Center

- Cryopyrin-associated periodic syndrome (https://rarediseases.info.nih.gov/diseases/10927/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Cryopyrin-associated periodic syndromes %22)

Catalog of Genes and Diseases from OMIM

- FAMILIAL COLD AUTOINFLAMMATORY SYNDROME 1; FCAS1 (https://omim.org/entry/120100)
- MUCKLE-WELLS SYNDROME; MWS (https://omim.org/entry/191900)
- CINCA SYNDROME; CINCA (https://omim.org/entry/607115)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%22Cryopyrin-associated+periodic+syndromes%22+%5Bti%5D)

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