

Cryopyrin-Associated Periodic Syndromes (CAPS): Patient Backgrounder

TOPICS:

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It is only quite recently that medical researchers have identified and described a new group of rare, inherited conditions known as Cryopyrin-Associated Periodic Syndromes or CAPS. For decades, doctors have seen patients experiencing the same unexplained symptoms of recurrent fever, rash, and joint pain but have not been able to pinpoint what disease was affecting their patients. With advancements in DNA testing and analysis, scientists now can differentiate CAPS from other similar disease sin many, but not all, patients, which will hopefully lead to the development of more effective treatments for this underserved population.

There are three related conditions that make up the broader disorder known as CAPS. These are:

- Familial Cold Auto-Inflammatory Syndrome (FCAS), also know as Familial Cold Urticaria
- Muckle-Wells Syndrome (MWS)
- Neonatal-Onset Multisystem Inflammatory Disease (NOMID), also referred to as Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA).

These diseases are classified as auto-inflammatory diseases and share a number of common symptoms, namely recurrent fever, rash, and joint pain. FCAS is the most common form of CAPS. NOMID is the most debilitating subtype of CAPS but is very rare. In its most severe form, patients with CAPS can experience hearing and vision loss, mental retardation, significant bone deformities, or kidney failure. The discovery of a new gene mutation in many patients has opened a brand new understanding of CAPS in recent years.

CAPS Generally Caused By a Gene Mutation

In 2001, researchers found that CAPS are generally caused by mutations or changes in a gene named the Cold-Induced Auto-Inflammatory Syndrome 1 (or CIAS1) gene, now named the Nod-Like Receptor Protein-3 (NLRP-3) gene. The CIAS1/NLRP-3 gene codes for a protein known as cryopyrin. In turn, this cryopyrin protein regulates the production of factors involved in helping the body fight off foreign invaders. One important factor is interleukin-1 β which circulates throughout the body and can trigger inflammation, or swelling. Researchers have found that mutations in the CIAS1/NLRP-3 gene cause the cryopyrin protein to produce too much interleukin-1 β . This overproduction leads to the development of symptoms of inflammation such as fever/chills, rash, joint pain, fatigue, and eye pain/redness that are prevalent in CAPS.

The CIAS1/NLRP-3 gene mutation is said to be autosomal dominant which is one of several ways that a disorder can be passed down through families. That means that if a person has just one copy of this version of the abnormal gene, he or she is extremely likely to develop one of the CAPS conditions. This also means that patients with CAPS have a 50 percent chance of having a child with this disorder.

What is an Auto-Inflammatory Disease and How is It Different From an Auto-Immune Disease?

The purpose of the immune system is to respond to foreign organisms in the body such as bacteria or viruses. When a foreign organism is detected in the body, the immune system produces antibodies (chemicals that identify and destroy the invading organisms). Auto-immune diseases such as rheumatoid arthritis, diabetes, and lupus occur when the antibodies that are released to fight these foreign organisms also attack healthy tissues; this destruction of healthy tissue causes inflammation. In auto-inflammatory disease, such as CAPS, the body spontaneously produces substances that cause inflammation without the formation of antibodies.

Types of CAPS and Common Symptoms

The three subtypes that comprise CAPS include Familial Cold Auto-Inflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), and Neonatal-Onset Multisystem Inflammatory Disease (NOMID). All are characterized by recurrent rash, fever/chills, joint pain, fatigue, and eye pain/redness.

Patients with FCAS develop these symptoms, within several hours after exposure to cooling temperatures, and the symptoms usually persist up to 24 hours. Patients with MWS (and those with NOMID) demonstrate these

same symptoms, but the symptoms are not necessarily related to exposure to cooling temperatures in these patients. In addition, MWS patients (and rarely FCAS patients) may develop hearing loss and are at risk for decreased kidney function due to deposits of protein in the kidney – a condition called renal amyloidosis. NOMID patients often develop severe central nervous system complications, including vision loss, mental retardation, and a type of swelling of the membrane covering the brain and spinal cord known as chronic aseptic meningitis, as well as severe joint and bone deformities. CAPS symptoms usually first appear during infancy or early childhood.

Diagnosis & Treatment

Diagnosis of CAPS is determined through an evaluation of a patient's symptoms and medical history. Confirmation of the diagnosis is achieved in many patients through genetic testing and the identification of a CIAS1/NLRP-3 mutation. Not all CAPS patients have a detectable genetic mutation. While there are no medications currently indicated for the treatment of CAPS, patients with FCAS often find some relief from symptoms with warming treatments like using blankets or taking hot baths to control their disease exacerbation. They may also try taking non-steroidal anti-inflammatory drugs such as aspirin or ibuprofen to help with joint pain. Medications commonly used to control inflammation such as high-dose corticosteroids and disease-modifying anti-rheumatic drugs have also been tried. Hearing aids can be used to correct the hearing loss that often occurs during adolescence in patients with MWS. There are currently no therapies approved by the U.S. Food and Drug Administration for the treatment of CAPS.

Talking to Your Physician

CAPS are a group of rare diseases. However, some scientists believe that CAPS could be more prevalent due to possible misdiagnoses. For example, CAPS symptoms often are seen in other more common diseases such as systemic juvenile idiopathic arthritis (formerly known as juvenile rheumatoid arthritis) and lupus. In addition, the larger class of auto-inflammatory disease known as Hereditary Periodic Fever Syndromes can act similarly to some forms of CAPS. To better understand whether a diagnosis of CAPS should be considered, there are a few questions you and your physician can ask:

- Have you suffered from recurrent symptoms such as rash, fever/chills, joint pain, fatigue, and eye pain/redness for most of your life, either beginning at infancy or early childhood?
- Is the rash that you experience something that appears on a large portion of your body?
- Do you have other family members that have similar symptoms?
- Does a decrease in room temperature or exposure to cooling/cold temperatures trigger symptoms to occur?

If you answered “yes” to these questions, a discussion about CAPS with your physician may be warranted.