Cryopyrin-Associated Periodic Syndromes (CAPS): Overview

TOPICS:

What Causes CAPS?

What Is an Autoinflammatory Disease and How Does It Differ From an Autoimmune Disease?

Diagnosing CAPS

Talking with Your Healthcare Provider

Cryopyrin-Associated Periodic Syndromes (CAPS) are a group of rare, inherited, autoinflammatory diseases. CAPS may be challenging to diagnose because the symptoms are often similar to those of other disorders.

There are 3 subtypes of CAPS:

- Familial Cold Autoinflammatory Syndrome (FCAS)
- Muckle-Wells Syndrome (MWS)
- Neonatal-Onset Multisystem Inflammatory Disease (NOMID) (also called Chronic Infantile Neurologic Cutaneous Articular, or CINCA, Syndrome)

These subtypes are classified as autoinflammatory diseases and share a number of common symptoms, including rash, fever/chills, joint pain, fatigue, and eye redness/pain. These symptoms may occur frequently. Symptom flares (episodes of more intense symptoms) may be triggered by cooling temperatures, stress, exercise, or unknown causes.

In its most severe form, CAPS can cause hearing and vision loss, mental impairment, significant bone deformities, or kidney failure.

The discovery of a gene mutation in some patients with CAPS has led to a greater understanding of CAPS and to the development of medications to relieve symptoms.

What Causes CAPS?

CAPS are generally caused by changes (mutations) in a gene called *NLRP3* (nucleotide-binding domain, leucine-rich family [NLR] pyrin domain containing 3). This gene, formerly called *CIAS1* (cold-induced autoinflammatory syndrome 1), is active in circulating, infection-fighting white blood cells. The *NLRP3* gene controls the production of cryopyrin, a protein that regulates the production of another protein called interleukin-1 beta (IL-1β).

As part of the immune system, IL-1β circulates throughout the body and can trigger inflammation, or swelling. Researchers have found that mutations in the *NLRP3* gene cause cryopyrin to produce too much IL-1β. This overproduction leads to symptoms of inflammation such as rash, fever/chills, joint pain, fatigue, and eye redness/pain.

The *NLRP3* gene is autosomal dominant, meaning that a person inheriting a copy of the mutated gene may develop CAPS. Children of CAPS patients who have the genetic mutation have a 50% chance of inheriting the mutated gene. But CAPS has also been reported in families with no history of the disease (meaning that it was not inherited but occurred spontaneously).

Because mutations in the *NLRP3* gene have been found in only half of patients with CAPS, scientists think that additional mutations may exist. Genetic testing alone may not be enough for a healthcare provider to diagnose CAPS.

What Is an Autoinflammatory Disease and How Does It Differ From an Autoimmune Disease?

Autoinflammatory diseases have symptoms that may resemble those of autoimmune diseases. However, the underlying autoinflammatory diseases are characterized by an inflammatory reaction that is seemingly unprovoked—no obvious causes or triggers can be identified. Recurrent episodes occur, with signs and symptoms that vary by disease.

The immune system responds to foreign organisms, such as bacteria or viruses, in the body. When a foreign organism is detected in the body, the immune system produces antibodies—chemicals that identify and destroy the foreign organisms. Autoimmune diseases such as rheumatoid arthritis, diabetes, multiple sclerosis, and lupus occur when antibodies that are released to fight these foreign organisms also attack healthy tissue. This destruction of healthy tissue causes inflammation.

Diagnosing CAPS

The symptoms of CAPS may be difficult to diagnose. Diagnosis may be delayed because CAPS are rare and the symptoms often resemble those of other disorders. Generally, healthcare providers confirm a diagnosis of CAPS through a combination of procedures. These include evaluation of a patient's symptoms and medical history, laboratory and genetic testing, and skin biopsy. Although the diagnosis is confirmed in many patients through genetic testing and the identification of *NLRP3* mutations, not all patients with CAPS have a detectable genetic mutation.

Talking with Your Healthcare Provider

CAPS are a group of rare diseases. However, some scientists believe that CAPS may be more common because of misdiagnoses. For example, CAPS-like symptoms are often seen in other, more common diseases such as systemic juvenile idiopathic arthritis (formerly called juvenile rheumatoid arthritis) and lupus. In addition, the larger class of autoinflammatory diseases called hereditary periodic fever syndromes can be similar to some forms of CAPS.

Answers to the following questions may help your healthcare provider when he or she evaluates your symptoms:

- Have you suffered from recurrent symptoms such as rash, fever/chills, joint pain, fatigue, and eye redness/pain for most of your life, beginning either at infancy or during early childhood?
- How often do these symptoms happen?
- How long do these symptoms last?
- How many days per month do you have these symptoms?
- What triggers your symptoms? Cold temperatures? Exercise? Stress?
- What helps your symptoms go away?
- Do you have other family members who have similar symptoms?