Blau Syndrome

Subjects: Genetics & Heredity
Contributor: Catherine Yang

Blau syndrome is an inflammatory disorder that primarily affects the skin, joints, and eyes. Signs and symptoms begin in childhood, usually before age 4.

Keywords: genetic conditions

1. Introduction

A form of skin inflammation called granulomatous dermatitis is typically the earliest sign of Blau syndrome. This skin condition causes a persistent rash that can be scaly or involve hard lumps (nodules) that can be felt under the skin. The rash is usually found on the torso, arms, and legs.

Arthritis is another common feature of Blau syndrome. In affected individuals, arthritis is characterized by inflammation of the lining of the joints (the synovium). This inflammation, known as synovitis, is associated with swelling and joint pain. Synovitis usually begins in the joints of the hands, feet, wrists, and ankles. As the condition worsens, it can involve additional joints and restrict movement by decreasing the range of motion in many joints. In people with Blau syndrome, the tendons as well as the joints can be inflamed, causing tenosynovitis.

Most people with Blau syndrome also develop uveitis, which is swelling and inflammation of the middle layer of the eye (the uvea). The uvea includes the colored portion of the eye (the iris) and related tissues that underlie the white part of the eye (the sclera). Uveitis can cause eye irritation and pain, increased sensitivity to bright light (photophobia), and blurred vision. Other structures in the eye can also become inflamed, including the outermost protective layer of the eye (the conjunctiva), the tear glands, the specialized light-sensitive tissue that lines the back of the eye (the retina), and the nerve that carries information from the eye to the brain (the optic nerve). While individuals with Blau syndrome may have normal vision, inflammation of any of these structures can lead to severe vision impairment or blindness.

Some individuals with Blau syndrome develop kidney disease (nephritis) due to inflammation. They may also have deposits of calcium in the kidneys (nephrocalcinosis) and often develop chronic kidney failure. Inflammation of blood vessels (vasculitis) can cause scarring and tissue death in the vessels and impedes blood flow to tissues and organs.

Less commonly, Blau syndrome can affect other parts of the body, including the liver, spleen, lymph nodes, brain, blood vessels, lungs, and heart. Inflammation involving these organs and tissues can impair their function and cause life-threatening complications. Rarely, affected individuals have disturbances in nerve function (neuropathy), episodes of fever, or high blood pressure in the blood vessels that carry blood from the heart to the lungs (pulmonary hypertension).

2. Frequency

Blau syndrome is a very rare disorder. It is estimated to affect fewer than 1 in 1 million children worldwide.

3. Causes

Blau syndrome results from mutations in the *NOD2* gene. The protein produced from this gene helps defend the body from foreign invaders, such as viruses and bacteria, by playing several essential roles in the immune response, including inflammatory reactions. An inflammatory reaction 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.

The *NOD2* gene mutations that cause Blau syndrome result in a NOD2 protein that is overactive, which can alter immune responses and trigger an abnormal inflammatory reaction. However, it is unclear how overactivation of the NOD2 protein causes the specific pattern of inflammation affecting the joints, eyes, and skin that is characteristic of Blau syndrome.

3.1. The Gene Associated with Blau Syndrome

- NOD2

4. Inheritance

Blau syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most affected individuals have one parent with the condition.

In some cases, people with the characteristic features of Blau syndrome do not have a family history of the condition. Some researchers believe that these individuals have a non-inherited version of the disorder called early-onset sarcoidosis.

5. Other Names for This Condition

- arthrocutaneouveal granulomatosis
- early-onset sarcoidosis
- familial granulomatosis, Blau type
- familial juvenile systemic granulomatosis
- granulomatous inflammatory arthritis, dermatitis, and uveitis, familial
- pediatric granulomatous arthritis

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