

Nakajo-Nishimura Syndrome

Subjects: Genetics & Heredity

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Nakajo-Nishimura syndrome is an inherited condition that affects many parts of the body and has been described only in the Japanese population. Beginning in infancy or early childhood, affected individuals develop red, swollen lumps (nodular erythema) on the skin that occur most often in cold weather; recurrent fevers; and elongated fingers and toes with widened and rounded tips (clubbing).

Keywords: genetic conditions

1. Introduction

Later in childhood, affected individuals develop joint pain and joint deformities called contractures that limit movement, particularly in the hands, wrists, and elbows. They also experience weakness and wasting of muscles, along with a loss of fatty tissue (lipodystrophy), mainly in the upper body. The combination of muscle and fat loss worsens over time, leading to an extremely thin (emaciated) appearance in the face, chest, and arms.

Other signs and symptoms of Nakajo-Nishimura syndrome can include an enlarged liver and spleen (hepatosplenomegaly), a shortage of red blood cells (anemia), a reduced amount of blood cells called platelets (thrombocytopenia), and abnormal deposits of calcium (calcification) in an area of the brain called the basal ganglia. Intellectual disability has been reported in some affected individuals.

The signs and symptoms of Nakajo-Nishimura syndrome overlap with those of two other conditions: one called joint contractures, muscular atrophy, microcytic anemia, and panniculitis-induced lipodystrophy (JMP) syndrome; and the other called chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome. All three conditions are characterized by skin abnormalities and lipodystrophy. Although they are often considered separate disorders, they are caused by mutations in the same gene, and some researchers believe they may represent different forms of a single condition.

2. Frequency

Nakajo-Nishimura syndrome appears to be rare and has been described only in the Japanese population. About 30 cases have been reported in the medical literature.

3. Causes

Nakajo-Nishimura syndrome is caused by mutations in the *PSMB8* gene. This gene provides instructions for making one part (subunit) of specialized cell structures called immunoproteasomes, which are found primarily in immune system cells. Immunoproteasomes play an important role in regulating the immune system's response to foreign invaders, such as viruses and bacteria. One of the primary functions of immunoproteasomes is to help the immune system distinguish the body's own proteins from proteins made by foreign invaders, so the immune system can respond appropriately to infection.

Mutations in the *PSMB8* gene greatly reduce the amount of protein produced from the *PSMB8* gene, which impairs the normal assembly of immunoproteasomes and causes the immune system to malfunction. For unknown reasons, the malfunctioning immune system triggers abnormal inflammation that can damage the body's own tissues and organs; as a result, Nakajo-Nishimura syndrome is classified as an autoinflammatory disorder.

Abnormal inflammation likely underlies many of the signs and symptoms of Nakajo-Nishimura syndrome, including the nodular erythema, recurrent fevers, joint problems, and hepatosplenomegaly. It is less clear how mutations in the *PSMB8* gene lead to muscle wasting and lipodystrophy. Studies suggest that the protein produced from the *PSMB8* gene may

play a separate role in the maturation of fat cells (adipocytes), and a shortage of this protein may interfere with the normal development and function of these cells.

3.1. The Gene Associated with Nakajo-Nishimura Syndrome

- PSMB8

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- ALDD
- autoinflammation, lipodystrophy, and dermatosis syndrome
- Japanese autoinflammatory syndrome with lipodystrophy
- JASL
- Nakajo syndrome
- NKJO

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