Adenosine Deaminase 2 Deficiency

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Adenosine deaminase 2 (ADA2) deficiency is a disorder characterized by abnormal inflammation of various tissues. Signs and symptoms can begin anytime from early childhood to adulthood. The severity of the disorder also varies, even among affected individuals in the same family.

Keywords: genetic conditions

1. Introduction

Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria). However, ADA2 deficiency causes abnormal, unprovoked inflammation that can damage the body's tissues and organs, particularly blood vessels. (Inflammation of blood vessels is known as vasculitis.) Other tissues affected by abnormal inflammation can include the skin, gastrointestinal system, liver, kidneys, and nervous system. Depending on the severity and location of the inflammation, the disorder can cause disability or be life-threatening.

Signs and symptoms that can occur with ADA2 deficiency include fevers that are intermittent, meaning they come and go; areas of net-like, mottled skin discoloration called livedo racemosa; an enlarged liver and spleen (hepatosplenomegaly); and recurrent strokes affecting structures deep in the brain that can start in the first few years of life. In some people, ADA2 deficiency causes additional immune system abnormalities that increase the risk of bacterial and viral infections.

ADA2 deficiency is sometimes described as a form of polyarteritis nodosa (PAN), a disorder that causes inflammation of blood vessels throughout the body (systemic vasculitis). However, not all researchers classify ADA2 deficiency as a type of PAN.

2. Frequency

More than 160 individuals with ADA2 deficiency have been described in the medical literature. However, researchers suspect that many more people may be affected, and ADA2 deficiency may not be a rare disease. They are working to determine whether this condition could underlie other, more common forms of vasculitis and stroke whose causes are currently unknown.

3. Causes

ADA2 deficiency is caused by mutations in the *ADA2* gene. This gene provides instructions for making an enzyme called adenosine deaminase 2. Studies suggest that this enzyme plays an essential role in the growth and development of certain immune system cells, including macrophages, which are a type of white blood cell that plays a critical role in inflammation. Some macrophages are pro-inflammatory, meaning they promote inflammation, while others are anti-inflammatory, meaning they reduce inflammation.

Mutations in the *ADA2* gene severely reduce or eliminate the activity of adenosine deaminase 2. Researchers do not fully understand how a shortage (deficiency) of this enzyme's activity leads to vasculitis and immune system abnormalities. They speculate that the enzyme deficiency may disrupt the balance between pro-inflammatory and anti-inflammatory macrophages in various tissues, leading to a buildup of pro-inflammatory macrophages and abnormal inflammation.

3.1. The gene associated with Adenosine deaminase 2 deficiency

- ADA2

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

- ADA2 deficiency
- childhood-onset polyarteritis nodosa
- DADA2
- deficiency of ADA2
- Sneddon syndrome

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