Carbonic Anhydrase VA Deficiency

Subjects: Genetics & Heredity
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Carbonic anhydrase VA deficiency is an inherited disorder characterized by episodes during which the balance of certain substances in the body is disrupted (known as metabolic crisis) and brain function is abnormal (known as acute encephalopathy). These potentially life-threatening episodes can cause poor feeding, vomiting, weight loss, tiredness (lethargy), rapid breathing (tachypnea), seizures, or coma.

genetic conditions

1. Introduction

During an episode, people with carbonic anhydrase VA deficiency have excess ammonia in the blood (hyperammonemia), problems with acid-base balance in the blood (metabolic acidosis and respiratory alkalosis), low glucose in the blood (hypoglycemia), and reduced production of a substance called bicarbonate in the liver. These imbalances lead to the signs and symptoms that occur during the episodes.

People with carbonic anhydrase VA deficiency typically first experience episodes of the disorder by age 2. These episodes may be triggered by going without food (fasting) for longer than usual between meals or when energy demands are increased, such as during illness. Between episodes, children with carbonic anhydrase VA deficiency are generally healthy, and more than half have no further episodes after the first one. Some affected children have mildly delayed development or learning disabilities, while others develop normally for their age.

The risk of metabolic crisis and acute encephalopathy is thought to decrease after childhood. Because of the small number of people with carbonic anhydrase VA deficiency who have come to medical attention, the effects of this disorder in adults are not well understood.

2. Frequency

The prevalence of carbonic anhydrase VA deficiency is unknown. Only a small number of affected individuals have been described in the medical literature. However, the disorder may be underdiagnosed because the metabolic crisis often does not recur after the first episode; researchers suspect that some babies diagnosed with transient hyperammonemia may actually have carbonic anhydrase VA deficiency.

3. Causes

Carbonic anhydrase VA deficiency is caused by mutations in the *CA5A* gene. This gene provides instructions for making the carbonic anhydrase VA enzyme, which helps convert carbon dioxide to a substance called bicarbonate. Bicarbonate is necessary to maintain the proper acid-base balance in the body, which is necessary for most biological reactions to proceed properly. The carbonic anhydrase VA enzyme is particularly important in the liver, where it provides bicarbonate needed by four enzymes in the energy-producing centers of cells (mitochondria). These enzymes help control the amount of various other substances in the body.

Mutations in the *CA5A* gene result in absent or impaired carbonic anhydrase VA enzyme function, leading to reduced bicarbonate production. Insufficient bicarbonate results in impaired control of acid-base balance and reduces the activity of the four affected mitochondrial enzymes, resulting in the various biochemical abnormalities associated with carbonic anhydrase VA deficiency. These imbalances cause acute encephalopathy and the other signs and symptoms associated with this disorder. Studies suggest that a related enzyme produced from the *CA5B* gene may increasingly compensate for the lack of carbonic anhydrase VA as affected individuals mature, which may result in a reduced risk of metabolic crisis and acute encephalopathy after childhood.

3.1. The Gene Associated with Carbonic Anhydrase VA Deficiency

- CA5A

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.

Some people who have two copies of the altered gene never develop the condition, a situation known as reduced penetrance. Researchers suggest that if people with these mutations get through the vulnerable period of childhood without having an episode of encephalopathy, they may never show signs or symptoms of the disorder.

5. Other Names for This Condition

- CA-VA deficiency
- CA5AD
- hyperammonemia due to carbonic anhydrase VA deficiency
- hyperammonemic encephalopathy due to carbonic anhydrase VA deficiency
- mitochondrial carbonic anhydrase va deficiency

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