What is pyruvate dehydrogenase deficiency, PDHA1-related?

Pyruvate dehydrogenase deficiency is an inherited neurodegenerative disease characterized by lactic acidosis, delayed development, and neurological problems. Individuals with pyruvate dehydrogenase deficiency, PDHA1-related, have defects in a component of the pyruvate dehydrogenase complex, which is needed to convert energy from food into a form that cells can use. When pyruvate builds up in cells, it is converted to lactic acid. Signs and symptoms of pyruvate dehydrogenase deficiency are due to decreased energy and the buildup of lactic acid in cells, which has the most severe consequences in the brain.

What are the symptoms of pyruvate dehydrogenase deficiency, PDHA1-related, and what treatment is available?

Pyruvate dehydrogenase deficiency, PDHA1-related, is a disease that varies in age of onset and severity. Signs and symptoms usually appear shortly after birth and may include:

- Lactic acidosis (buildup of lactic acid)
- Nausea and vomiting
- Severe breathing problems
- Abnormal heartbeat
- Developmental delay
- Intellectual disability
- Seizures
- Hypotonia (poor muscle tone)
- Ataxia (loss of muscle coordination)
- Abnormal brain structures

Many individuals with pyruvate dehydrogenase deficiency, PDHA1-related, do not survive past childhood, although some may live into adolescence or adulthood. There is no cure and treatment is supportive.

How is pyruvate dehydrogenase deficiency, PDHA1-related, inherited?

Pyruvate dehydrogenase deficiency can be caused by mutations in at least five genes, including PDHA1, which is responsible for approximately 80% of cases. Pyruvate dehydrogenase deficiency, PDHA1-related, is an X-linked disease. A male who inherits one copy of a PDHA1 gene mutation is affected with pyruvate dehydrogenase deficiency. A female who inherits one copy of a PDHA1 mutation is a carrier and may have some symptoms.

If a female is a carrier, the risk for each son to be affected is 50% and the risk for each daughter to be a carrier is 50%. If a male is affected, each son is unaffected and each daughter is an obligate carrier.

Who is at risk for pyruvate dehydrogenase deficiency, PDHA1-related?

Pyruvate dehydrogenase deficiency, PDHA1-related, is a rare condition that can occur in individuals of all races and ethnicities. Its prevalence is unknown.

Having a relative who is a carrier or who is affected can increase an individual’s risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.
What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?


National Organization for Rare Disorders (NORD): http://rarediseases.org/rare-diseases/pyruvate-dehydrogenase-complex-deficiency/

Children Living with Inherited Metabolic Diseases (CLIMB): http://www.climb.org.uk/

References