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My46 Trait Profile

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes

Mitochondria are small organelles that exist in every cell of the body. They are like the powerhouse of the cells and produce the energy our bodies need to function. Symptoms of mitochondrial disease are usually most present in the organs that require the most energy like the muscles, brain, and heart. Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes is a mitochondrial disorder that can cause progressive muscle weakness and neurological problems, elevated levels of lactate in the blood and spinal fluid, and episodes of metabolic stroke. It is most commonly caused by a mutation in the MT-TL1 gene that makes a mitochondrial transfer RNA molecule.

Characteristics of Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes

Individuals with Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes (MELAS) can have a wide range of symptoms including fatigue, muscle weakness, seizures, high levels of lactate in the blood or spinal fluid, headaches, difficulty gaining weight, problems with vision or hearing, enlargement of the heart muscles (cardiomyopathy), and cognitive difficulties. The signs and symptoms of MELAS are highly variable within families as well as between other unrelated, affected individuals. The symptoms may be very mild or very severe. They may appear later in life or get progressively worse over time. Individuals with MELAS are at risk for metabolic strokes. Metabolic strokes have similar symptoms to typical (vascular) strokes and may cause problems walking, talking, or seeing, but they look differ from vascular strokes on brain imaging tests (e.g., MRIs). Metabolic strokes require immediate medical attention. People with MELAS may recover completely from the strokes or may have long-term effects after a stroke.

Diagnosis/Testing

MELAS is caused by a change or mutation in the mitochondrial DNA. There are two sets of genetic material in the body: mitochondrial DNA and nuclear DNA. Mitochondrial DNA (mtDNA) tells the mitochondria how to function. Nuclear DNA also helps with mitochondrial function, but also codes for instructions for the rest of the body. MELAS is commonly caused by a single mutation (m.3243A>G) in the mitochondrial gene MT-TL1, but it can also be caused by other changes in the mitochondrial DNA. A healthcare provider may order genetic testing for MELAS if there is a family history of the condition or if an individual has symptoms that seem like they could be due to MELAS.

Management/Surveillance

Individuals with MELAS need to be care for by providers who are familiar with their condition. It is recommended that they have routine vision and hearing screenings. Additionally, many individuals with mitochondrial disease may have heart problems, and should be regularly evaluated by a cardiologist. Individuals with mitochondrial disease may have increased symptoms of their disease during times of illness, especially when they are vomiting or not eating or drinking well. Periods of long illness require immediate medical attention. Individuals with MELAS should also inform their providers if they are undergoing surgery or a medical procedure that requires them to fast, as this can also worsen symptoms.

Individuals with MELAS should be closely monitored for signs of stroke including sudden vision loss, muscle weakness, severe headache, slurred speech, or confusion. When there is concern of a stroke, individuals with MELAS

often have a brain MRI imaging study to confirm the stroke. Individuals with MELAS may need services such as physical, occupational, or speech therapy. It is important that healthcare providers monitor individuals with MELAS syndrome on a regular basis for disease progression. Many individuals with MELAS take a vitamin compound with coenzyme Q10 and other vitamins that may increase the mitochondria's ability to produce energy. They may take arginine supplements to help prevent strokes.

It is recommended that valproic acid, a medication often prescribed for seizure management, be avoided in individuals with MELAS.

Mode of inheritance

Mitochondria are structures inside the cells that are responsible for generating the energy that is needed to perform daily activities. Humans also carry DNA in mitochondria, and mutations in mitochondrial DNA can result in MELAS.

Humans inherit mitochondria only from their mothers. Therefore, in maternal mitochondrial inheritance, the affected mitochondria are passed from mothers (who may or may not show symptoms) to children of either sex. Because males do not transmit mitochondria, a male with a maternal mitochondrial disorder generally cannot pass it to his children. Mitochondrial DNA mutations can also occur brand new (de novo) in an affected individual. When de novo, parents and siblings of an affected person are not at increased risk, but if the affected person is a female, her children are at increased risk.

Inside each cell, there is a mixture of mutated mitochondrial DNA and normal mitochondrial DNA. Symptoms are more likely when the mixture contains more mutated mitochondrial DNA. The number of mitochondria with mutated versus a normal mitochondrial DNA is variable across different body tissues (blood, brain, heart, skin, hair, etc.). Moreover, the number of mutated versus normal mitochondrial DNA can change dramatically when passed from mothers to their children.

Risk to family members

Maternal mitochondrial inheritance is associated with a significant degree of variability. Because of this remarkable variability, it can be difficult to provide inheritance risk estimates for people with a maternal mitochondrial condition; however specific information may be available depending on the identified mitochondrial DNA mutation. Mothers of individuals with MELAS usually have the mtDNA mutation, and thus all siblings of the individual with MELAS also have the mtDNA mutation. The exact risk for these individuals to develop symptoms is unknown.

Special considerations

None

Resources

MitoAction
http://www.mitoaction.org
United Mitochondrial Disease Foundation
http://www.umdf.org/site/c.8qKOJ0MvF7LUG/b.7929671/k.BDF0/Home.htm
Genetics Home Reference: Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes
http://ghr.nlm.nih.gov/condition/mitochondrial-encephalomyopathy-lactic-acidosis-and-stroke-like-episodes

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