Mitochondrial Myopathy Encephalopathy Lactic Acidosis and Stroke-Like Episodes

MELAS, MELAS syndrome

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes Syndrome, also known as MELAS, is a rare mitochondrial condition where the body is not able to make enough mitochondrial proteins needed to make energy. Mitochondria are parts of a cell that help turn the energy we get from food into energy that the body can use. They are also important in the communication between body parts and creating other materials the body needs. Mitochondrial conditions can cause a variety of signs and symptoms in many parts of the body, particularly those that use a lot of energy like muscles and the brain.

Genetics

MELAS is an inherited genetic condition, meaning it is passed down in a family. MELAS is caused by changes in the mitochondrial genome (mtDNA) or set of DNA contained in the mitochondria of a cell. Mitochondria are inherited from the mother through her eggs. People typically do not inherit any mitochondria from sperm, making it very unlikely for mitochondrial conditions to be passed down from a father. Both males and females can have MELAS.

Changes, sometimes called mutations or variants, in several genes can cause MELAS. These include *MT-ND1*, *MT-ND5*, *MT-TH*, *MT-TL1*, and *MT-TV*.

Frequency

While MELAS is a rare disorder, it is one of the more common mitochondrial conditions. It is estimated that approximately one in 4000 people have MELAS, but the exact frequency varies by country. MELAS may also be underdiagnosed.

Signs and Symptoms

MELAS can cause a range of signs and symptoms. These can present at any age, but most often appear in childhood following a period of normal development. The exact features, onset, and severity can vary widely among people with this condition, even among members of the same family. Always check with your provider if new symptoms appear or you are concerned.

Signs and symptoms may include:

- Weakness and pain
- Recurrent headache
- Loss of appetite
- Vomiting
- Seizures
- Uncontrolled movements (ataxia)
- Diabetes
- Mental health conditions
- Gastrointestinal or kidney conditions

Most people with MELAS have a stroke-like episode before age 40. These episodes often involve temporary muscle weakness on one side of the body, called hemiparesis, altered consciousness, vision changes, seizures and severe headaches that can seem like a migraine.
Repeated stroke-like episodes can lead to brain damage, vision loss, problems with movement, and loss of intellectual abilities (dementia).

Most people with MELAS have a buildup of lactic acid in their bodies, a condition called lactic acidosis. Increased acidity in the blood can lead to vomiting, abdominal pain, extreme tiredness or fatigue, muscle weakness, and difficulty breathing. Less commonly, people with MELAS may experience involuntary muscle spasms called myoclonus, impaired muscle coordination (ataxia), hearing loss, heart and kidney problems, diabetes, and hormonal imbalances.

Diagnosis

MELAS can be diagnosed by:
- Muscle biopsy showing ragged red fibers (RRF)
- SDH staining showing overabundance of mitochondria in smooth muscle and blood vessels
- Measuring biochemical markers in blood or the cerebrospinal fluid (fluid surrounding the brain and spinal cord)
- Brain studies and imaging looking for changes in the structure of the brain or seizure activity (MRI, MRS, EEG)
- Heart studies looking for rhythm changes (EKG)
- Performing a genetic test to look for changes in the genes known to cause MELAS

MELAS is not included on newborn screening panels. If there is a known family history of MELAS, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta). Results interpretation of this testing for mitochondrial conditions is complicated and genetic counseling is recommended.

Treatment and Management

Before beginning any treatment or therapy, please consult with your physician.

As of 2022, there is no FDA-approved therapy for MELAS. Treatment and management of MELAS is symptomatic and supportive.

This may include:
- Traditional medications for seizures (antiepileptic drugs)
- Physical therapy and aerobic exercise to support muscle function
- Traditional treatment of heart conditions
- Hearing aids or cochlear implants for hearing loss
- Avoidance of mitochondrial toxins like certain drugs, tobacco, and alcohol
- Mitochondrial supplements like riboflavin and Coenzyme Q10
- Traditional treatment of diabetes
- Traditional treatment for migraines

People with MELAS typically work with several healthcare providers regularly, including:
- Neurology for the muscles and brain
- Ophthalmology for the eyes
- Cardiology for the heart
- Audiology for hearing
- Endocrinology for hormones and blood sugars

Since illness with fever can trigger presentation of MELAS symptoms, people with MELAS are encouraged to receive standard childhood vaccinations, flu vaccine, and pneumococcal vaccine. It is important that all those living with or caring for someone with Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-Like Episodes Syndrome have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during a crisis and in emergency room settings.

Clinical Trials

For specific details on clinical trials visit www.mitoaction.org/clinicaltrials or www.clinicaltrials.gov.

Resources

- Mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes - About the Disease – The National Institutes of Health
- MELAS Syndrome - National Organization for Rare Disorders)

Connecting with others who are impacted by a rare disease allows for important information to be

shared about day-to-day life, prevents isolation, and gives hope. Please contact MitoAction for peer support opportunities at 888-MITO-411 or email mito411@mitoaction.org.

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