Mitochondrial DNA Depletion Syndrome

MDS

Mitochondrial DNA depletion syndrome, also known as MDS, is a group of genetic conditions affecting the mitochondria. For those with MDS, there isn't enough mitochondria in certain tissues or body parts. 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. Different types of MDS can affect one part of the body or many parts of the body.

Genetics

MDS is a group of genetic conditions caused by changes, sometimes called mutations or variants, in many genes. Both males and females can have MDS. MDS can either be passed down in a family, known as inherited, or can result from a new genetic change in a baby, called de novo.

People usually have two copies of most genes, one inherited from each parent. Recessive conditions occur when there are changes in both copies of a gene. When inherited, MDS is usually autosomal recessive. If only one copy of a gene is changed, a person is considered a carrier and is usually not symptomatic. If both parents are carriers, there is a one in four chance with each pregnancy that their child will have the condition.

Frequency

MDS is thought to be extremely rare. The most common form, due to genetic changes in the gene TK2, has been reported in fewer than 100 people around the world.

Signs and Symptoms

MDS can cause a range of additional signs and symptoms. These can present as a baby and progress rapidly with early death due to respiratory failure. Others have a later childhood onset and may have slowly progressive muscle weakness.

Theexact features, onset, and severity can vary widely between people who have the condition, even among members of the same family. Always check with your doctor if new symptoms appear or you are concerned.

Signs and symptoms may include:

- Muscle weakness (myopathy or hypotonia) or loss of muscle control (ataxia)
- Trouble breathing (respiratory failure)
- Developmental delay or inability to meet developmental milestones (failure to thrive)
- A buildup of lactic acid in the body (lactic acidosis)
- Liver problems
- Feeling of "pins and needles" or loss of sensation (neuropathy)
- Feeding difficulty
- Seizures or epilepsy

Diagnosis

MDS can be diagnosed by:

- Measuring biochemical markers in blood and cerebrospinal fluid (the fluid surrounding the brain and spinal cord)
- Testing a sample from the muscle or liver (biopsy)

- Performing a genetic test

MDS is not included on newborn screening panels. If there is a known family history of a MDS, 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 any MDS. Treatment and management of MDS is symptomatic and supportive.

This may include:

- Liver transplant
- Traditional treatment of heart and kidney conditions
- Hearing aids or cochlear implants for hearing loss
- Physical and occupational therapy
- Avoidance of mitochondrial toxins like certain drugs, tobacco, and alcohol
- Mitochondrial supplements

People with MDS typically work with several healthcare providers regularly depending on their symptoms including:

- Neurology for the muscles and brain
- Ophthalmology for the eyes
- Cardiology for the heart
- Nephrology for the kidneys
- Audiology for hearing
- Gastroenterology for the pancreas, stomach, and intestines
- Endocrinology for hormones and blood sugar
- Transplant team if a liver transplant is needed

It is important that all those living with or caring for someone with Mitochondrial DNA Depletion 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 Depletion Syndrome - Children's Hospital of Philadelphia

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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