Mitochondrial Neurogastrointestinal Encephalopathy

MNGIE, polyneuropathy, ophthalmoplegia, leukoencephalopathy, and intestinal pseudo-obstruction (POLIP); oculogastrointestinal muscular dystrophy (OGIMD); and mitochondrial myopathy with sensorimotor polyneuropathy, ophthalmoplegia, and pseudo-obstruction (MEPOP)

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Mitochondrial Neurogastrointestinal Encephalopathy, also known as MNGIE, is a rare mitochondrial condition where errors in the mitochondrial genome (the set of DNA contained in a cell's mitochondria) build up over time in different tissues. 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 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

MNGIE is an inherited genetic condition, meaning it is passed down in a family. People usually have two copies of the *TYMP* gene (formerly known as *ECGF1*), one inherited from each parent. MNGIE occurs when there are changes in both copies of the *TYMP* gene (autosomal recessive inheritance). Someone who has a change in only one copy of the *TYMP* gene is called a carrier, and they usually do not have any medical symptoms. If both parents are carriers, there is a 1 in 4 chance with each pregnancy that their child will have MNGIE. Both males and females can have MNGIE.

Frequency

The exact frequency of MNGIE is not known. It is thought to be very rare. More than 120 people with clinical features of MNGIE have been described in the medical literature, though this condition may be underdiagnosed.

Signs and Symptoms

MNGIE can cause a range of signs and symptoms typically beginning before age 20 (though onset can range from 5-60 years). 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:

- GI concerns may include: vomiting, nausea, diarrhea, abdominal pain, a feeling of early fullness (premature satiety), stomach rumblings (borborygmi), difficulty swallowing (dysphagia), and small sac-like protrusions (diverticula) of the inner intestines
- GI complications may include: bacterial overgrowth and/or failure of the intestines to absorb nutrients during digestion (malabsorption). This can lead to weight loss as well as loss of tissue and muscle mass (cachexia). People with MNGIE are typically extremely thin and some have short stature.
- Numbness, tingling, or pain in the arms and legs (sensory neuropathy)
- Muscle weakness
- Drooping of the upper eyelid (ptosis) and weakness of other muscles around the eye which can restrict movements (ophthalmoplegia)
- Loss of the myelin sheath that covers nerve fibers in the brain (leukoencephalopathy) observed on imaging. This is usually not associated with symptoms.
- Hearing loss
- Changes in the electrical signals of the heart (cardiac conduction defects)

Diagnosis

MNGIE can be diagnosed by:

- Measuring biochemical markers in blood like lactate and pyruvate
- GI studies depending on symptoms (both imaging and exploratory procedures)
- Brain studies and imaging looking for changes in the structure of the brain (MRI)

- Heart studies looking for rhythm changes (EKG)
- Nerve studies (nerve conduction velocity study/NCV) to look for nerve function
- Liver and kidney studies to assess how well they are working
- Performing a genetic test to look for changes in genes known to cause MNGIE

MNGIE is not included on newborn screening panels. If there is a known family history of MNGIE, or if parents know they are carriers of MNGIE, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta).

Treatment and Management

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

There is currently no FDA-approved therapy for MNGIE. Treatment and management of MNGIE are symptomatic and supportive. This may include:

- Traditional treatment of GI symptoms with antibiotics for bacterial overgrowth
- Careful monitoring of swallowing ability and airways
- Nutrition support
- Physical therapy and occupational therapy
- 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
- Special schooling arrangements

People with MNGIE typically work with several healthcare providers regularly based on their symptoms, including:

- Gastroenterology (for the stomach, intestines, and swallowing)
- Dieticians (for feeding support)
- Neurology (for the muscles and brain)
- Physical and occupational therapy (for strength and mobility)
- Ophthalmology (for the eyes)
- Cardiology (for the heart)
- Audiology (for hearing)

All those living with or caring for someone with MNGIE must have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during crises and in emergency room settings.

Clinical Trials

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

Resources

- Mitochondrial neurogastrointestinal encephalopathy syndrome - The National Institutes of Health
- Mitochondrial Neurogastrointestinal Encephalopathy - National Organization for Rare Disorders
- Mitochondrial Neurogastrointestinal Encephalopathy Disease - GeneReviews
- What is Mitochondrial Neurogastrointestinal Encephalopathy? - ThinkGenetic, Inc

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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