Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver disease

Other Names: Hypermanganesemia with dystonia, polycythemia, and cirrhosis

*Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver disease* is a genetic syndrome in which affected individuals typically have trouble talking (dysarthria) and walking (dystonia) because of an accumulation of manganese (a mineral) in the body. It is caused by mutations in the SLC30A10 gene which makes a protein called zinc transporter 10.

**Characteristics of Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver disease**

Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver disease is an inherited condition that has only been identified in a handful of families in the world. Individuals with this condition usually have extremely high levels of manganese in their blood. Manganese is a mineral in the body that is necessary for normal functioning. However, too much manganese in the body can be harmful, particularly to the liver and brain. Although the condition can present differently within and between families, most untreated individuals have manganese levels over 2000 nmol/L in the blood -- individuals without this condition typically have levels less than 320 nmol/L.

Manganese accumulation in the brain can lead to difficulty with talking (dysarthria) and with movement. The movement problems seen in this condition include difficulty walking, tremor, bradykinesia (i.e., slow movement), and parkinsonism symptoms (i.e., shuffling walk, rigidity, bradykinesia, and loss of facial expression). Manganese accumulation in the liver can lead to an enlarged liver (hepatomegaly) and scarring of the liver (i.e., cirrhosis). Individuals with this condition often also have an accumulation of too many red blood cells (polycythemia) in the bloodstream. Intelligence is usually normal in individuals with dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease.

**Diagnosis/Testing**

In the handful of families identified worldwide, affected individuals have changes or mutations in a gene called SLC30A10, which makes the zinc transporter 10 protein. This protein is thought to play an important role in manganese processing in the body. Mutations in the SLC30A10 gene prevent the protein from working properly, thus allowing manganese to accumulate to harmful levels in the liver and brain.

**Management/Surveillance**

Management of dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease includes a regular injection of a medication (disodium calcium edetate) that can help remove the excess manganese (i.e., chelation therapy) from the body. Iron supplements can also help decrease the levels of manganese by reducing uptake of manganese. A helpful way to understand this is to think of musical chairs: if more people representing iron are in the room competing for the same chairs as the people who represent manganese, then the people who represent manganese are less likely to get a chair than those representing iron. This “competitive binding” is also the reason that iron levels are low in individuals with excess manganese; the iron simply does not get used by the body because it cannot compete with
the high levels of manganese. In the small number of families with this condition, chelation therapy and iron therapy have shown to be effective particularly with significantly improving speech and movement.

Blood tests are regularly performed to monitor liver enzymes, manganese levels, and blood cell counts. Brain and liver imaging tests (e.g., MRIs and ultrasounds) can help monitor the levels of manganese.

Foods and spices containing high amounts of manganese such as cloves, saffron, wheat, nuts, mussels, dark chocolate, and seeds should be avoided.

Individuals having trouble walking, talking, writing, or otherwise moving can consider physical therapy, occupational therapy, and/or speech therapy.

Mode of inheritance

Dystonia/Parkinsonism, Hypermanganesemia, Polycythemia, and Chronic Liver disease is inherited in an autosomal recessive pattern. This means that an individual has to inherit two SLC30A10 mutations (i.e., one from each parent) to be affected with the condition. If both parents are carriers of a SLC30A10 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease.

Risk to family members

Parents of a child with dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease are carriers of the condition. If a sibling of a child with dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease is unaffected, he/she has a 66% (or 2/3) chance of being a carrier of dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease.

Special considerations

Although the movement problems seen in dystonia/parkinsonism, hypermanganesemia, polycythemia, and chronic liver disease can mimic Parkinson’s disease, the typical treatment for Parkinson’s disease (levodopa medication) does not appear to be effective in treating individuals with high levels of manganese.

Resources

WE MOVE: Worldwide Education and Awareness for Movement Disorders
http://www.wemove.org

Genetics Home Reference: Hypermanganesemia with dystonia, polycythemia, and cirrhosis

References


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