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My46 Trait Profile

Mucopolysaccharidosis Type 3

Other Names: Sanfilippo syndrome

Mucopolysaccharidosis type 3 is a genetic condition characterized by the body's inability to break down complex sugar molecules called glycosaminoglycans. It is caused by mutations in the GNS, HGSNAT, NAGLU, and SGSH genes, each of which makes a enzyme involved in breaking down these large molecules.

Characteristics of Mucopolysaccharidosis Type 3

Individuals with mucopolysaccharidosis type III (MPS III) cannot properly break down complex sugar molecules called glycosaminoglycans (GAGs) because a particular enzyme is not working properly. Without enough enzyme, GAGs build up in various tissues of the body. As the GAGs accumulate, disease symptoms become debilitating and life threatening. There are four forms of MPS III: MPS IIIA, MPS IIIB, MPSIIIC, and MPS IIID. The features seen are the same in all forms, but they each have a different genetic cause.

Newborns with MPS III usually have no features of the condition. Signs and symptoms often start to appear from 1 to 4 years of age. Initial signs include delays in development, extreme activity, restlessness, severe behavioral problems, and sleep disturbances (e.g., affected children may sleep very little at night). As the condition progresses, language and understanding, as well as the ability to walk is gradually lost. Affected children can also experience frequent seizures, and swallowing difficulties. Osteoporosis can develop as early as the teen years, decreasing stability and increasing the risk of fractures. Hearing loss is also a common problem, often due to frequent ear infections.

Diagnosis/Testing

A diagnosis of MPS III can be made by measuring the level of enzyme activity from a blood sample. A person with MPS III often has deficient (low) enzyme activity. A diagnosis of MPS IIIA can be made by measuring the sulfamidase enzyme activity from a blood sample. A diagnosis of MPS IIIB can be made by measuring the alpha-N-acetylglucosaminidase enzyme activity from a blood sample. A diagnosis of MPS IIIC can be made by measuring the heparan-alpha-glucosaminide N-acetyltransferase enzyme activity from a blood sample. A diagnosis of MPS IIID can be made by measuring the N-acetylglucosamine-6-sulfatase enzyme activity from a blood sample.

A diagnosis of MPS III can also be done by genetic testing for changes or mutations in the SGSH (causing MPS IIIA), NAGLU (causing MPS IIIB), HGSNAT (causing MPS IIIC), and GNS (causing MPS IIID). These genes make enzymes that are responsible for breaking down specific GAGs. Mutations in these genes prevent the enzymes from working properly, resulting in a build-up of specific GAGs in various organs of the body.

Management/Surveillance

Management of MPS III often involves physical, occupational, and speech therapies to maintain function as long as possible. Over the counter medications may be helpful for problems with diarrhea and constipation, and high-dose vitamin D therapy may improve bone mineral density. Unfortunately medications typically used for hyperactivity tend not be beneficial for children with MPS III. However, low-dose melatonin may help with sleep problems. Seizures can usually be prevented or reduced in frequency with conventional anti-seizure medications. Although heart problems are rare in MPS III, an annual echocardiogram is recommended. As swallowing becomes more difficult, families often consider an alternative means of feeding, such as through a gastrostomy tube (G-tube). Developmental testing is helpful

for managing expectations and school placements.

There are no FDA approved treatments for MPS III, although there are clinical trials for MPS IIIA gene therapy and enzyme replacement therapy (ERT). Future clinical trials are planned for MPS IIIB ERT and gene therapy, and research for additional treatments in MPS III is promising.

Mode of inheritance

MPS III is inherited in an autosomal recessive pattern. This means that an individual has to inherit two mutations (i.e., one from each parent) to be affected with MPS III. If both parents are carriers of a mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with MPS III.

Risk to family members

Parents of a child with MPS III are carriers of MPS III. If a sibling of a child with MPS III is unaffected, he/she has a 2 in 3 (or 66%) chance of being a carrier of MPS III.

Special considerations

None

Resources

National MPS Society
http://www.mpssociety.org
Genetics Home Reference: Mucopolysaccharidosis type III
http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-iii

References

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