Mucolipidosis IV

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Synonyms of Mucolipidosis IV

- Berman Syndrome
- Ganglioside Neuraminidase Deficiency
- Ganglioside Sialidase Deficiency
- ML Disorder IV
- ML IV
- Neuraminidase Deficiency
- Sialolipidosis

Disorder Subdivisions

- No subdivisions found.

General Discussion
Mucolipidosis IV is a rare inherited metabolic disorder believed to be characterized by a deficiency of transport channel receptor protein, based upon the recent discovery of the Mucolipidosis IV gene. This deficiency may lead to the accumulation of certain fatty substances (mucolipids) and certain complex carbohydrates (mucopolysaccharides) within the cells of many tissues of the body.

Mucolipidosis IV is characterized by mental retardation; severe impairment in the acquisition of skills requiring the coordination of muscular and mental activities (psychomotor retardation); diminished muscle tone (hypotonia); clouding (opacity) of the clear portion of the eyes through which light passes (cornea); and/or degeneration of the nerve-rich membrane lining the eyes (retinal degeneration). Mucolipidosis IV is thought to be inherited as an autosomal recessive genetic trait.

Symptoms

The symptoms and physical findings associated with Mucolipidosis IV are usually apparent within three to eight months following birth. The first recognized symptom usually is clouding (opacity) of the clear portion of the eyes through which light passes (cornea). In some cases, this may not be apparent until three to five years of age.

Most affected infants exhibit diminished muscle tone (hypotonia); moderate to severe mental retardation; delays in reaching developmental milestones; and/or significant delays in the acquisition of skills requiring the coordination of muscular and mental activities (psychomotor retardation).

In addition to opacities of the cornea, individuals with Mucolipidosis IV may have additional abnormalities affecting the eyes including crossed eyes (strabismus), puffy eyelids, degeneration of the nerve-rich membrane lining the eyes (retina), and/or visual impairment (amblyopia) in an eye that appears structurally normal. In some cases, such eye abnormalities may result in an abnormal sensitivity to light (photophobia) and/or nearsightedness (myopia).

Individuals with Mucolipidosis Type IV develop iron deficiency anemia because their stomachs do not secrete acid. They do not have enlarged livers or spleens, skeletal involvement, or mucopolysaccharides in the urine.

Causes

Mucolipidosis Type IV is inherited as an autosomal recessive genetic trait. Recently, the responsible gene was isolated and its protein-product, as well as its chromosomal location, determined. The gene has been tracked to 19p13.3-p13.2 where it encodes
for the mucolipin-1 protein. It is designated as the MCOLN1 gene.

Chromosomes are found in the nucleus of all body cells. They carry the genetic characteristics of each individual. Pairs of human chromosomes are numbered from 1 through 22, with an unequal 23rd pair of X and Y chromosomes for males and two X chromosomes for females. Each chromosome has a short arm designated as p and a long arm identified by the letter q. Chromosomes are further subdivided into bands that are numbered. For example, chromosome 11p15.4 refers to band 15.4 on the short arm of chromosome 11.

Human traits including the classic genetic diseases, are the product of the interaction of two genes for that condition, one received from the father and one from the mother.

In recessive disorders, the condition does not appear unless a person inherits the same defective gene for the same trait from each parent. If an individual receives one normal gene and one gene for the disease, the person will be a carrier for the disease, but usually will not show symptoms. The risk of transmitting the disease to the children of a couple, both of whom are carriers for a recessive disorder, is 25 percent. Fifty percent of their children risk being carriers of the disease, but generally will not show symptoms of the disorder. Twenty-five percent of their children may receive both normal genes, one from each parent, and will be genetically normal (for that particular trait). The risk is the same for each pregnancy.

Researchers suspect that the symptoms of Mucolipidosis Type IV develop due to deficiency of a transport protein. Cells take up metabolites from the environment. In the case of certain fatty substances (mucolipids) and certain complex carbohydrates (mucopolysaccharides), these products of metabolism must be transported within the cell to the lysosomes where these complex substances are further broken down into simpler components. If these complex substances are not transported within the cell to the factories in which they are further broken down, they accumulate within the cells with disastrous effects. It is the accumulation of the substances within the cell that is the cause of Mucolipidosis IV. These substances accumulate because of a lack, within the cells, of the protein necessary for the transportation process. Researchers believe that this cell-deficiency may lead to the symptoms of this disorder due to the abnormal accumulation of the complex chemical compounds within the cells of many tissues of the body.

Affected Populations
Mucolipidosis Type IV is a rare inherited metabolic disorder that affects males and females in equal numbers. The disorder was first identified in 1974. About one-half of the reported individuals with Mucolipidosis Type IV are of Ashkenazi Jewish parentage. The exact incidence is unknown with approximately 70 cases reported in the medical literature.

**Related Disorders**

N/A

**Standard Therapies**

**Diagnosis**
A carrier test is now available to screen for the Mucolipidosis IV gene. Mucolipidosis IV may be diagnosed before birth (prenatally) by means of a procedure known as amniocentesis. During amniocentesis, a small portion of the fluid that surrounds the fetus (amniotic fluid) is removed; cells from the fluid are then tested in the laboratory for the Mucolipidosis IV gene.

A diagnosis of Mucolipidosis Type IV may also be confirmed based upon a thorough clinical examination, a detailed patient history, and a variety of specialized tests. In most cases, an electron microscope is used to visualize characteristic lysosomal storage bodies in certain connective tissue cells (fibroblasts). Fibroblasts are usually obtained from biopsied tissue of the skin and/or the delicate membrane that lines the eyes (conjunctiva). As noted above, genetic testing has recently become available for diagnostic purposes. Individuals with ML-IV present with iron deficiency anemia, high serum gastrin levels and characteristic findings on brain MRI examinations.

**Treatment**
Treatment of Mucolipidosis Type IV is symptomatic and supportive. Symptoms associated with clouding of the corneas may be treated by the use of contact lenses and/or artificial tears. Genetic counseling will be of benefit for affected individuals and their families. Intense physical, occupational and speech therapy are also of benefit. Iron replacement is utilized for those with anemia.

**Investigational Therapies**

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving U.S. government funding, and some supported by private industry, are posted on this government website.

For information about clinical trials being conducted at the National Institutes of
Since prenatal diagnosis is now possible through amniocentesis, new treatments aimed at checking mucolipidosis IV are now under investigation. One method might involve replacing defective transport protein. Scientific study of gene replacement in animal models raises the hope that gene replacement therapy may someday be made available to people with genetic disorders such as mucolipidosis IV.

In a study sponsored by the National Institute of Neurological Disorders and Stroke (NINDS), scientists are investigating the natural history and causes of mucolipidosis IV. This study seeks to better understand the disease, identify the medical difficulties for patients, and discover improved methods of diagnosing mucolipidosis IV. Information on this clinical trial is available from the NIH sources listed above.

Organizations related to Mucolipidosis IV

- Genetic and Rare Diseases (GARD) Information Center
  
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  Gaithersburg, MD 20898-8126  
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  800 #: 888-205-2311  
  e-mail: N/A  

- Hide & Seek Foundation for Lysosomal Disease Research
  
  6475 East Pacific Coast Highway Suite 466  
  Long Beach, CA 90803  
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  Home page: [http://www.hideandseek.org](http://www.hideandseek.org)

- Madisons Foundation
References

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