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Mucopolysaccharidosis Type II (MPS II) Disease (Hunter Syndrome)

Information for Physicians and Other Health Care Professionals

Definition

MPS II disease, also referred to as Hunter syndrome, is an inherited, X-linked lysosomal storage disorder caused by deficiency in the activity of the enzyme iduronate-2-sulphatase (I2S). This enzyme is responsible for the breakdown of two different glycosaminoglycans (GAGs), dermatan sulfate and heparan sulfate. Lysosomal accumulation of these GAG molecules results in cell, tissue and organ dysfunction.

Clinical Symptoms

MPS II is a multisystem disorder and presents in two forms. The severe form, type A, is typically diagnosed in children aged 2-4 years, while the mild form, type B, may not be diagnosed until later. In type A, systems include developmental delay; hepatosplenomegaly; ivory-colored skin lesions; coarse facies; skeletal deformities, including short stature, short neck, broad chest and macrocephaly; joint stiffness and carpal tunnel syndrome; hyperactivity; recurrent ear infections with progressive hearing loss; progressive retinal degeneration; airway obstruction; cardiac valvular disease; and gastrointestinal problems, such as chronic diarrhea in younger patients and significant constipation later on in life. In type B, many of the same clinical symptoms are present, but in a milder form and type B patients usually have normal intelligence and do not have the severe skeletal problems of type A. Unlike Hurler syndrome (MPS I), corneal clouding is not seen in MPS II and clinical features may progress more slowly.

Newborn Screening and Definitive Diagnosis

In Illinois, newborn screening for MPS II disease is performed by measuring I2S enzyme activity. **If newborn screening results indicate abnormal activity of I2S enzyme, referral should be made to a metabolic disease specialist.**

Treatment

Once clinical findings appear, treatment of MPS II disease is multi-disciplinary and is best treated by a team of specialists knowledgeable about the disease who can offer supportive and symptomatic care. Care is directed toward relieving the symptoms and is not typically instituted until clinical symptoms appear. Enzyme replacement therapy is now available for MPS II and this treatment ameliorates the somatic features of the disorder but does not treat the central nervous system. Developmental, occupational and physical therapy are often necessary.

Incidence

The incidence of MPS II disease is unknown; however, the incidence, as determined by other newborn screening programs, ranges between one in 100,000 to one in 150,000 male births.

Inheritance Patterns

MPS II disease is an X-linked disorder. Although the disorder is variable in age of onset and severity, males inheriting the X-linked gene mutation are always affected. Females who inherit the gene for MPS II disease are not expected to be symptomatic. Sons born to carrier females have a 50 percent chance of being affected while

daughters have a 50 percent chance of being a carrier like their mother. Affected males will not pass the X-linked gene mutation to any of their sons; however, 100 percent of their daughters will be carriers of the X-linked MPS II disease. Genetic counseling is recommended for families planning future pregnancies.

Pathophysiology

In MPS II disease, the lack of iduronate-2-sulphatase (I2S) activity leads to an abnormal accumulation of two glycosaminoglycans (GAGs), dermatan and heparan sulfate. The build-up of GAGs in the lysosomes causes clinical findings of the disease.

Key Points for Parents

Reassure parents not all infants identified as having low I2S activity through newborn screening will have MPS II. If the infant should turn out to have MPS II, enzyme replacement therapy is available that may ameliorate the clinical symptoms of the disorder. If the child needs additional testing or diagnostic evaluation, make certain the parents understand the importance of following the pediatrician's and/or specialist's recommendations for additional testing and referrals.

Follow-up After Confirmation of Diagnosis

These guidelines should be followed after a diagnosis of MPS II disease has been confirmed:

1) Follow-up with the child's metabolic disease specialist.
2) Recommend genetic counseling services to help the parents understand the complexity surrounding the carrier state and inheritance of this disease.
3) Provide parents information on support services, such as the National MPS Society and the local health department.
4) Additional information about newborn screening can be found at:
    - Baby's First Test: http://www.babysfirsttest.org/
      Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.
    - National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov/gtr/
      National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.