MULTIPLE SULFATASE DEFICIENCY (MSD)

A PHYSICIAN'S GUIDE TO DIAGNOSIS

MSD is both a leukodystrophy and a lysosomal storage disorder. This ultra-rare fatal genetic disorder is currently reported in less than 100 cases globally.
MSD is caused pathogenic variants in both copies of the ***SUMF1*** gene located on chromosome 3. *SUMF1* is responsible for encoding a protein called formylglycine-generating enzyme (FGE), which post-translationally activates all 17 sulfatases, many of which are located in the lysosome of the cell. Individuals with MSD lack functional FGE which in turn leads to absent or decreased sulfatase levels and a build-up molecules with sulfate residues (sulfatides, glycosaminoglycans, etc.).

There are different subtypes of MSD: **Neonatal** form, **Late-infantile** form, and **Juvenile** form. The neonatal form is the most severe and can present in utero or at birth. These children often to decline very rapidly and often die during the first two years of life. Late-infantile form is seen most commonly in the population. Children with this form have normal cognitive development in the beginning of life, but then gradually begin to regress and lose skills. The final form, Juvenile, is the rarest. Individuals with this form typically do not show signs or symptoms until middle to late childhood and they have an overall slower loss of skills.

Prognosis:
Currently there is no treatment or cure for MSD; only palliative care is available. The average life expectancy is between 10-14 years.

- ✓ Autosomal recessive single gene disorder
- ✓ Necessitates continuous care
- ✓ Potential candidate for gene therapy (research ongoing)

Diagnosis for MSD:

Biochemical Testing: Diagnosis of MSD can occur through biochemical testing showing low activity levels of at least two sulfatase enzymes.

Genetic Testing: Individuals with MSD have biallelic pathogenic variants in the *SUMF1* gene which can be confirmed through molecular genetic testing.

Both of these methods can be used to diagnose MSD, however genetic testing is still recommended following a biochemical diagnosis to identify the specific *SUMF1* pathogenic variants.

**Note: This information is intended to be used as a guide for physicians when MSD is suspected, based on the experiences of parents and caregivers of children with MSD. The United MSD Foundation does not diagnose diseases, treat patients or offer specific medical advice.*

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Signs/Symptoms

There are a number of signs and symptoms experienced by patients with MSD. Symptoms can be divided by the different tissue types in which the waste material is building up. Below are some of the experienced symptoms in children with MSD, which typically present at around 18 months - 2 years of age when the child starts missing certain developmental milestones.

- Developmental delay
- Loss of neurological function
- Increased spasticity
- Scaley Skin; Excess Hair
- Hepatosplenomegaly
- Progressive skeletal dysplasia
- Blindness
- Loss of oral feeding (often requiring a g-tube)
- Hydrocephalus
- Loss of motor and communication skills
- "Coarse" facial features
- Dry skin on stomach, scalp and back

How is MSD Managed?

Management of MSD is largely based on the presenting symptoms. However, the MSD child's physician should expect the child to have multiple body systems affected, thus requiring a multidisciplinary team to provide care: Neurologist, Metabolist, Pediatrician, Gastroenterologist, Nutritionist, Urologist, Orthopedist, and Psychiatrist. Some services that might be recommended include speech, physical, and occupational therapies. To assist with developmental delays, early intervention should be recommended to families whenever possible.

Finally, physicians of MSD patients will need to continually observe for progression of the disease.

For More Information:

Multiple Sulfatase Deficiency requires continuous care and management. Parents and caregivers with children with MSD have resources for support available to them. For more information, contact the United MSD Foundation.

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