MAROTEAUX-LAMY SYNDROME

DESCRIPTION:

Maroteaux-Lamy syndrome (also called Mucopolysaccharidosis type 6) is one of the so-called "lysosomal overload" diagnoses, to which Morquio syndrome also belongs. Due to mutations in the ARSB gene, this progressive condition is characterized by a defect in the degradation of a mucopolysaccharide (sugar class) which, by accumulating in the body, often causes a notable short stature with many associated characteristics.
Growth ceases around the age of 6 or 8 years. In severe forms of the diagnosis, adult height is often close to 100 cm (3'3"). People with a moderate form of the dwarfism can reach 160 cm (5'3") in height.
This type of dwarfism is an autosomal recessive inherited trait [see "Genetics"]. It affects approximately 1 in 300,000 births.

CHARACTERISTICS AND DIAGNOSIS:

Maroteaux-Lamy syndrome is degenerative and very disabling. Fatalities due to cardiac and respiratory complications is often determined by the severity of the condition. The average life expectancy is 30 years.

This diagnosis, is a disproportionate type of dwarfism, with the following characteristics:

- Facial dysmorphia (thick eyebrows, lips, eyelids and earlobes);
- Macroglossia (thick tongue that forces children to keep their mouths open);
- Macrocephaly (larger head);
- Short neck and trunk;
- Curved fingers;
- Hernias (inguinal and abdominal);
- Greyish teeth, small and spaced.

Skeletal irregularities are present and become more pronounced as the child grows. These include platyspondyly (flattening of the vertebral body of several vertebrae), kyphosis (humpback), scoliosis, pectus carinatum (protruding sternum), genu valgum (knock-knees) and long bone deformity.

At birth, Maroteaux-Lamy syndrome is not visible. Clinical signs generally appear between 6 to 24 months of age, when the accumulation of dermatan sulfate causes a slowing of growth and the appearance of skeletal and facial characteristics. Radiological examination reveals deformities of the epiphyses (bone heads), coxa valga (malformation of the head of the femur), short and thick metacarpals (palm bones), underdevelopment of the ulna and radius

(forearm bones) and abnormalities of the ribs and spine.
The high presence of dermatan sulfate in the urine and the absence (or deficiency) of the enzyme arylsulfatase B in the blood confirms the diagnosis.
Genetic testing may also be used .

MAIN POSSIBLE COMPLICATIONS:

Eyes: Opacity of the cornea is common. This is a common phenomenon that leads to a progressive loss of vision. Risks of photophobia are present. Glaucoma or cataracts may also appear, as well as retinal degeneration.
Sight should be evaluated every one to two years. In children over 10 years of age, the evaluation should include tonometry (measurement of eye pressure).

Teeth and tongue: Cysts frequently form where permanent teeth are supposed to grow, preventing normal eruption of the teeth and possibly causing severe pain.
In addition, macroglossia (thick tongue) makes chewing and swallowing difficult. There is a risk of choking on food. Speech and language therapy can help children swallow food safely. Parents can also learn some techniques to help the affected person avoid choking. In some cases, a gastrostomy (placing a tube through the skin and stomach lining) will be necessary to allow the child to eat safely.

Hearing problems: Middle ear problems are the cause of progressive hearing loss, which is aggravated by recurring ear infections. Hearing loss, which usually occurs in childhood, is present in almost everyone with Maroteaux-Lamy syndrome.
Consequently, a hearing evaluation must be performed annually from the time of diagnosis. If necessary, a myringotomy (insertion of a ventilation tube into the eardrum) may be performed.

Abdomen and hernias: The abdomen is often bulky and swollen. Hepatomegaly (enlargement of the liver) and splenomegaly (enlargement of the spleen) are usually present, and may cause discomfort and pain.
In addition, children frequently have one or more hernias in the groin (inguinal hernia) or navel (umbilical hernia). Often present at birth, they are one of the first signs of the diagnosis. Hernias can be corrected by surgery, but there is a risk of recurrence.

Carpal tunnel syndrome: This condition is very common, and is due to the compression of the nerves of the hand at the wrist. If not treated quickly, it causes numbness and tingling, then subsequently pain in the hand and even in the elbow. Without treatment, the forearm muscles eventually weaken.

Hydrocephalus (excess cerebrospinal fluid in the brain): It is important to watch for hydrocephalus, as it can cause an increase in intracranial pressure that, if left untreated, can lead to serious damage of the central nervous system.
Signs of increased pressure inside the skull are headaches, vomiting or nausea, visual disturbances, disturbances in alertness and consciousness (drowsiness, attention problems, apathy, etc.).
The installation of a shunt, to drain the fluid out of the cranial cavity, is necessary in some cases.

Neck (cervical spine): The small size of the neck and the accumulation of mucopolysaccharides can cause compression of the spinal cord.
Symptoms to watch for are neck pain and stiffness in the neck. The lower and upper limbs may be affected. The person may experience muscle weakness, numbness, decreased fine motor skills, difficulty walking and balancing, functional impotence, sphincter disorders (incontinence, dysuria, polycythemia and sometimes stress incontinence). If left untreated, compression can lead to paralysis and bladder control problems.

It is therefore necessary to have x-rays and MRI (magnetic resonance imaging) tests of the cervical region as soon as the diagnosis is made, and then every year thereafter. In case of symptoms, a surgeon specializing in spinal disorders will be able to perform cervical decompression (with or without fusion).

Heart: Heart damage, related to the accumulation of mucopolysaccharides, is common. Hypertension is quite common. Regurgitation or valve blockage may also occur. Valvulopathy can progress slowly over a period of years with no apparent clinical effect. If the problem worsens, it will probably be necessary to replace the damaged valves through surgery (valvuloplasty). Although rare, cardiomyopathy can develop.
The most common symptoms of valvulopathy are discomfort, chest tightness or pressure, palpitations, shortness of breath, fatigue, weakness and dizziness.
Because of cardiac risks, a cardiological and echocardiographic evaluation should be performed when Maroteaux-Lamy syndrome is diagnosed, and preferably every one or two years thereafter.

Respiratory system: Obstructive and restrictive lung involvement is common and may cause shortness of breath, loss of endurance, recurrent episodes of pneumonia as well as sleep apnea.
Sleep related breathing issues should be monitored, as it is a sign of respiratory failure that can lead to cardiovascular complications. Obstructive sleep apnea is characterized by loud snoring, apneic pauses, compensatory sighs, enuresis ("bed-wetting"), nocturnal vomiting, and irritability or drowsiness during the day [see "Sleep Apnea" fact sheet].

As a preventive measure, lung function tests should begin in childhood and should be repeated every one or two years. In addition, to avoid pulmonary complications from

infections, all individuals should be regularly vaccinated against influenza and pneumococcal disease. Tonsils and adenoids may also be assessed, and ventilation devices should be used at night.

Anesthesia: The risks of complications are many and increased due to the cervical, respiratory and cardiac complications associated with Maroteaux-Lamy syndrome.
In the event of an operation, it is therefore necessary to be sure to call upon the services of an experienced anesthetist [see the "anesthesia" section].

TREATMENT:

Treatment aims to improve the patient's quality of life and to slow down the progression of the condition. It is multidisciplinary and involves pediatricians, surgeons, orthopedists, cardiologists, dentists, speech-language pathologists, pneumologists, cardiologists, physiotherapists and ophthalmologists.

In addition, two main treatments are currently available for Maroteaux-Lamy syndrome. The first, enzyme replacement therapy, marketed under the name Naglazyme® (galsulfase), provides enough enzymes to partially break down the mucopolysaccharides accumulated in the cells. The enzyme is administered weekly by infusion, throughout the life of the affected person.

The second therapy, based on the transplantation of hematopoietic (bone marrow-derived) stem cells, is less often used.
Finally, a third approach, gene therapy, is currently under study.

List of the main elements to be monitored and managed [see the sheet "frequent interventions in short people"]:

- Eye, hearing and dental problems;
- Risk of choking on food;
- Abdominal hernias;
- Carpal tunnel syndrome;
- Hydrocephalus;
- Cervical spinal cord compression;
- Cardiac and respiratory problems.

RESOURCES:

Association québécoise des personnes de petite taille
https://www.aqppt.org/

Little People of Ontario
https://littlepeopleofontario.com/

Regroupement québécois des maladies orphelines - Centre iRARE
https://rqmo.org/centre-dinformation-et-de-ressources-en-maladies-rares/

Orphanet – fact sheet on Maroteaux-Lamy Syndrome
https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=24&Disease_Disease_Search_diseaseGroup=maroteaux-lamy&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group%20of%20diseases=Mucopolysaccharidosis-type-6&title=Mucopolysaccharidosis%20type%206&search=Disease_Search_Simple

NORD - National Organisation for Rare Disorders
https://rarediseases.org/rare-diseases/maroteaux-lamy-syndrome/

Society for Mucopolysaccharide Diseases, *A Guide to Understanding Maroteaux-Lamy Disease (MPS VI),* 2013
http://www.mpssociety.org.uk/wp-content/uploads/2016/07/guide-mps_vi-2013-web.pdf

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