METATROPIC DYSPLASIA

DESCRIPTION :

The term "metatropic", which means "variable" in Greek, refers to the changing nature of the condition of the bone development over time. This constitutional bone diagnosis is caused by mutations in the *TRPV4* gene, which code for a protein involved in the development of bone and cartilage. Affected people therefore see their height impacted; average height in adulthood ranges from 107 cm (3'6 in) to 135 cm (4'5 in).

Metatropic dysplasia is an autosomal dominant trait (a child of an affected parent has a one in two chance of being impacted) [refer to "genetics" factsheet]. However, in some cases it is a *de novo* genetic mutation, meaning that the child is born to parents of average height. The prevalence of the condition is unknown.

CHARACTERISTICS AND DIAGNOSIS :

Metatropic dysplasia causes severe disproportionate dwarfism. During infancy, the trunk is long and the limbs are short, then spinal involvement with progressive kyphoscoliosis results in an inversion of the proportions in adulthood. This changing aspect of morphology is typical of the condition. Here are the main physical characteristics:

- Kyphoscoliosis (double irregularity combining a hunchback curvature and a three-dimensional twist of the spine);
- High forehead and root of the nose flattened and widened, square jaw;
- Chest issues including a narrow chest and short ribs (later in childhood);
- Short and stocky hands and feet (later in childhood);
- Shortening of the trunk (later in childhood);
- Bowing of the limbs in varus (outward) or valgus (inward);
- Protruding joints (later in childhood);
- Hypermobility of small joints (fingers);
- Contractures of the large joints (knees and hip).

The condition is often discovered at birth due to the shortening of the limbs, the length and narrowness of the trunk, and the presence of kyphoscoliosis. The size of newborns, however, is close to average size.

The x-rays show in particular a platyspondyly (flattening of the bones of the spine), a pelvis in the shape of a halberd, a shortening of the diaphyses (body of the bones) and an enlargement of the metaphyses (growth plate located under the head of the bone). A genetic test identifying the mutation of the *TRPV4* gene can confirm the diagnosis.

MAIN POSSIBLE COMPLICATIONS :

Hydrocephalus (excess cerebrospinal fluid in the brain): Present in 5 to 29% of cases, is often benign. However, in some cases placing a bypass to drain the fluid out of the brain is necessary (surgery). Watch for hydrocephalus and learn to recognize the signs of increased intracranial pressure to avoid serious health outcomes.
These signs include headache, vomiting or nausea, visual problems and disturbances in alertness and consciousness (drowsiness, problems with attention, listlessness, etc.).

Bowing of the legs (varus or valgus): It is important to monitor the alignment of the limbs and the presence of chronic pain.
In the event of severe misalignment, an osteotomy (surgical section of the long bones) is recommended.

Kyphoscoliosis: Often present from birth, this curvature of the back must be treated as soon as it is detected because of its potential severity and the complications it generates. A clinical evaluation must therefore take place every six months. It must be accompanied by x-rays, or even an MRI (magnetic resonance imaging).
Treatment of kyphoscoliosis is difficult. Brace support is generally insufficient and often only delays surgery (fusion).

Instability of the cervical spine: It is not always present, but if it is, it should be monitored, as it can lead to spinal cord compression. Monitoring includes cervical x-rays in flexion and extension positions.
Symptoms to monitor: Neck pain, stiff neck. Both lower and upper limbs can be affected. Muscle weakness, numbness, decreased fine motor skills, gait and balance disorders, functional impotence, sphincter disorders (incontinence, dysuria, pollakiuria and sometimes stress incontinence). If the compression is not taken care of, it can lead to paralysis and problems with bladder control.
If the instability is severe, surgery (cervical decompression with fusion) will be necessary.

Respiratory Issues: Irregularities of the spine, thorax and ribs cause decreased lung function and respiratory distress which can be fatal.
Occlusion of the upper and lower airways are common. Affected individuals breathe hard and have hyperextension of their neck. In particular, you should monitor for breathing disorders at night while they sleep, as they are a sign of respiratory failure which can cause cardiovascular complications. Obstructive sleep apnea is characterized by loud snoring, apneic pauses, compensating sighs, new enuresis ("bedwetting"), nocturnal vomiting, and irritability or drowsiness during the day [refer to "sleep apnea" factsheet].
Because of the respiratory risks, pulmonary function monitoring should be carried out regularly from early childhood. Removal of tonsils and/or adenoids and the use of ventilators (CPAP or BiPAP) can help treat breathing problems at night. A tracheostomy will be necessary in some more serious cases.

Anesthesia: The risk of complications is particularly increased due to cervical, respiratory and neurological issues resulting from metatropic dysplasia.
In the event of an operation, an experienced anesthetist should be consulted and present. Finally, before implementing any invasive technique, it is necessary to have pulmonary function of the patient evaluated [refer to the "anesthesia" factsheet].

TREATMENT :

The treatment of metatropic dysplasia is essentially symptomatic and aims to prevent the progression of bone issues and the resulting problems (neurological, pulmonary, etc.). Treatment can include the use of orthopedic devices, physical therapy and surgical correction of skeletal abnormalities, which requires the collaboration of a team of specialists, including pediatricians, orthopedists, surgeons, neurologists, pulmonologists, physiatrists, etc.
Currently, there is no specific treatment for metatropic dysplasia. Growth hormones are not recommended.

List of the main elements to monitor and address [refer to the "Frequent interventions in little people" factsheet]:

- Bowing of the legs in varus or valgus;
- Risk of hydrocephalus;
- Kyphoscoliosis;
- Cervical instability with risk of spinal cord compression;
- Respiratory issues.

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
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=fr&Expert=2635

NORD – National Organisation for Rare Disorders
https://rarediseases.org/rare-diseases/metatropic-dysplasia-i/

GARD – Genetic and Rare Diseases Information Center
https://rarediseases.info.nih.gov/diseases/3571/metatropic-dysplasia

OMIM – Online Mendelian Inheritance in Man
https://www.omim.org/entry/156530?search=metatropic%20dysplasia&highlight=dysplasia%20metatropic%20dysplastic

Nemours – Children's Health System
https://www.nemours.org/services/skeletal-dysplasia/metatropic.html?tab=about&kidshealth=dwarfism

Association Québécoise des Personnes de Petite Taille

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