SPONDYLOEPIPHYSEAL DYSPLASIA

DESCRIPTION :

Spondyloepiphyseal dysplasia (SED) is a form of bone dysplasia, a general term for diagnoses characterized by atypical development of cartilage, bone, and/or growth. There are two main forms of spondyloepiphyseal dysplasia: congenital (SEDC) and tardive (SEDT; SEDL).

The more common congenital form is caused by a mutation in the COL2A1 gene. It causes a decrease in type 2 collagen levels, which leads to irregularities in skeletal growth. As a result, people with the condition are short in height, ranging from 84 cm to 128 cm (2'8" to 4'2") in adulthood. The diagnosis is an autosomal dominantly trait, but most cases are due to a new mutation (without a family history) [see "Genetics"].
It is estimated that the condition affects approximately 1 in 100,000 births.

The late form or tardive of spondyloepiphyseal dysplasia (SEDT; SEDL), which occurs between 6 and 10 years of age, can be transmitted in an X-linked recessive, autosomal recessive or autosomal dominant manner [see Genetics]. More commonly, the X-linked form results from a mutation in the SEDL gene (also known as TRAPPC2), which has an impact on cartilage formation. Women can be carriers of the condition, but it only occurs in men. Female carriers have a 50% chance that each of their offspring will be affected. Men with the diagnosis have no possibility that their children will be affected but are able to pass on the gene to their daughters.
Tardive spondyloepiphysis causes moderate dwarfism, so that affected men have an average height of 145 cm to 160 cm (4'9" to 5'3"). The X-linked form of the diagnosis affects about one in 150,000 to 200,000 births.

Since SEDT; SEDL is milder, the focus here is on the congenital form of SED. Where complications apply to the late form, this will be mentioned in square brackets. Finally, those who wish to learn more about the late form can consult the sources listed at the end of this fact sheet.

CHARACTERISTICS AND DIAGNOSIS :

Congenital spondyloepiphyseal dysplasia results in a disproportionately small stature where the arms appear long in relation to the torso. The main features of the condition include irregularities of the spine, joints, and abnormalities affecting the eyes. Characteristics include:

- A short barrel-shaped trunk;
- A protrusion of the sternum and ribs;

- Lordosis (hollow back), kyphosis (hunched back) and/or scoliosis;
- Joint abnormalities (coxa vara, genu varum, etc.);
- Club feet;
- Nearsightedness;
- And sometimes, a cleft palate (opening of the palate).

The condition is visible in newborns since skeletal issues and growth delay begins before birth. Skeletal irregularities affect the long bones of the arms and legs as well as the bones of the spine. X-rays reveal rounded and flattened vertebrae, as well as underdevelopment and fragmentation of the bone and cartilage of the epiphyses (bone heads). Genetic testing can confirm the diagnosis.

PRIMARY POSSIBLE COMPLICATIONS :

Cleft palate (opening of the palate): Present in some individuals with SEDC, cleft palate can lead to difficulties in swallowing and speaking. It can also cause middle ear problems. The ears and eardrums of infants with this issue should be monitored as early as nine or twelve months of age and every six months thereafter.
Surgery is available to correct cleft palate.

Clubfoot: Treatment should begin in the first few weeks of life. It includes softening and straightening of the foot and the application of bandages. Thereafter, the child will have to wear custom-made orthopedic shoes. If necessary, casts and/or surgery may also be performed.

Hydrocephalus (excess cerebrospinal fluid in the brain): Present in some children, it is benign. If an acceleration of the process is observed, neuroimaging may be performed. However, it should be noted that usually no treatment is indicated.

Hypotonia: Children under 2 years of age may suffer from muscle weakness causing delays in motor development (lifting the head, sitting, standing, walking, etc.). Some children may also have an unusual gait.
Muscle tone can be developed through physiotherapy exercises. Wearing a corset or brace may also be considered.

Hearing Issues: Middle ear dysfunction is the cause of progressive hearing loss, which is aggravated by recurring ear infections. The hearing loss, which usually occurs in childhood, is present in almost all people with congenital spondyloepiphyseal dysplasia. Therefore, a hearing assessment should be performed at 12, 18 and 24 months of age, and once a year thereafter. If necessary, a myringotomy (insertion of a ventilation tube into the eardrum) may be performed.



Eyes: Strong myopia is common. It is associated with a risk of retinal detachment. Therefore, an ophthalmologic evaluation should be performed during the first six months of life and then every 6 to 12 months. If retinal detachment is suspected, it is advisable to consult a specialist without delay, as it can have serious consequences on vision. Signs of retinal detachment include the sudden appearance or increase of floating bodies (filaments in the field of vision), flashes of light similar to flashes of lightning, blurred vision, or sudden loss of vision.

Leg issues: Genu varum (bowed legs) is common. The alignment of the legs, as well as the appearance of chronic knee pain and the limitation of walking should be monitored clinically. Surgery should be reserved for people with severe and symptomatic misalignment.

Hip degeneration [also in the tardive or late form]: The majority of people with spondyloepiphyseal dysplasia have early osteoarthritis of the hip. A coxa vara (irregularity of the femur) is also common.

Radiological monitoring should be carried out from the age of about 4 years, or even earlier if an issue is suspected. An osteotomy (surgery to repair bone and joint problems) may be performed if necessary; a total hip replacement (surgery to restore a damaged joint) will often be necessary around the age of 30 or 40.

Lordosis, scoliosis, kyphosis or kyphoscoliosis (combination of kyphosis and scoliosis) [also scoliosis in the tardive or late form]: The spine should be examined clinically every 6 months because of the high risk of early development of curvatures. X-rays can be taken in case of doubt. Lordosis can cause chronic and recurrent back pain. If there is pain, physical therapy based on exercises to strengthen the lower abdominal muscles and pelvic rotation exercises may have some benefit.

Scoliosis will often require orthotic treatment during childhood. It is important to act as soon as the first signs of an issue appears. A corset or brace can correct spinal curvatures, but in some cases, especially in the presence of kyphoscoliosis, surgical fusion will be necessary.

Neck (cervical spine) [also in the tardive or late form]: Cervical instability (hypermobility of the neck vertebrae) may be present. If this is the case, there is a risk of spinal cord compression, a problem that can lead to slow, gradual myelopathy (spinal cord injury) or paralysis.

The first signs of myelopathy are decreased muscle endurance and tone, hyperreflexia (exaggerated reflexes) and clonus (rapid contractions and reflexes of the limbs), especially in the legs, and problems with bowel and/or bladder control (incontinence, etc.).

Because of these risks, radiographic and/or MRI (magnetic resonance imaging) examinations of the cervical region must be performed as soon as the diagnosis of congenital spondyloepiphyseal dysplasia is made. Examinations should then be performed at regular intervals, even if the cervical spine appears stable, as there is a risk of subsequent instability.



In addition, a neurological examination should be performed at least once a year if there is no apparent instability on x-rays or MRIs, and more frequently if there is instability.
If problems are present, a surgeon specialized in spinal disorders should be consulted. If the instability is severe, cervical decompression with fusion will be required.

Respiratory system : Some infants may have difficulty breathing, especially if their rib cage is underdeveloped. Problems such as tracheomalacia or bronchomalacia may occur. Breathing may become wheezy or noisy and the person may quickly become short of breath. Infants will present with episodes of cyanosis (blue discolouration of the skin). The resulting respiratory failure can cause death, so it should be closely monitored.

Respiratory status should be assessed at birth. If wheezing increases and the child is experiencing respiratory distress, a pediatric pneumologist should be consulted. Breathing difficulties usually decrease as the infant grows older; however, in some cases, issues of the spine and an underdeveloped chest may cause breathing difficulties by preventing the lungs from filling completely (restrictive lung disease). This leads to chronic respiratory problems, sleep apnea, frequent respiratory infections, and heart failure in adulthood. Prompt and appropriate treatment can reduce this risk.

Anesthesia: There are risks, particularly related to the instability of the cervical spine, narrow airways and respiratory problems [see the "anesthesia" section].
It is therefore necessary to evaluate the stability of the cervical spine before any anesthesia. If instability is detected, an intubation with external stabilization of the neck should be performed. It will also be necessary to adapt the endotracheal tubes to the size of the individual (e.g. the size used for premature babies should be utilized for young children, and the pediatric size used for adults). Finally, delayed extubation may be necessary due to the low respiratory reserve in people with congenital spondyloepiphyseal dysplasia.

TREATMENT :

The management of spondyloepiphyseal dysplasia is multidisciplinary (surgery, orthopedics, occupational therapy, physiotherapy, ophthalmology, etc.) and preventive, and aims primarily at detecting complications.

Currently, there is no specific treatment for this condition. As an intrinsic abnormality of bone growth, the use of growth hormones is not effective in the treatment of spondyloepiphyseal dysplasia. Finally, limb lengthening, a controversial practice, is not recommended. Since this diagnosis affects the trunk and the spine; the disproportion may be aggravated if the limbs are lengthened. This technique can also negatively affect the joints, which are already weakened by the diagnosis.

List of the main elements to be monitored and managed [see the sheet "Frequent interventions for people of short stature"]:

- Cleft palate;
- Clubfoot;
- Hearing and eye issues;
- Leg issues;
- Osteoarthritis and degeneration of the hip [also in the late form];
- Curvatures of the spine [also in the tardive or late form];
- Instability of the cervical spine [also in the tardive or late form];
- Breathing issues.

RESOURCES :

- **General:**

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/

- **Congenital spondylo-epiphyseal dysplasia (SEDC):**

Little people of America - fact sheet on congenital spondylo-epiphyseal dysplasia
https://www.lpaonline.org/assets/documents/NH%20SEDC.pdf

NORTH - National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/spondyloepiphyseal-dysplasia-congenital/

Francis Veyckemans and Jean-Louis Scholtes, Syndrome and rare diseases in pediatrics: anesthesia, database available online:
https://sites.uclouvain.be/anesthweekly/MRP/index.html?DysplasieSpondyloepiphysaire.html

- **Tardive or Late spondylo-epiphysary dysplasia (SEDT; SEDL):**

Orphanet - fact sheet on Tardive Spondyloepiphysar Dysplasia
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=93284

Little people of America - fact sheet on late spondylo-epiphyseal dysplasia
https://www.lpaonline.org/assets/documents/NH%20SED%20TARDA.pdf

NORTH - National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/spondyloepiphyseal-dysplasia-tarda/

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