SILVER-RUSSELL SYNDROME

DESCRIPTION :

Silver-Russell (aka Russell-Silver) syndrome, a rare genetic diagnosis, is one of six conditions in the "primordial dwarfism" family. Different genetic variations are at the origin of this syndrome; in 60% of cases, the variations concern chromosomes 7 or 11; for the remaining 40%, the genetic cause remains unknown. In adulthood, the average height of men is 152 cm (4 ft 12 in) and that of women is 143 cm (4 ft 8 in).

The condition affects 1 in 30,000 to 100,000 births. In most cases, the syndrome occurs spontaneously, with no family history. In the other cases, it is an autosomal dominant trait, and sometimes an autosomal recessive trait [refer to the “genetics” factsheet].

CHARACTERISTICS AND DIAGNOSIS :

Silver-Russell syndrome causes dwarfism characterized by bodily asymmetry and relative macrocephaly (head that appears large in relation to the body). Other physical features of the syndrome include:

- A broad and rounded forehead;
- A small triangular face;
- Micrognathia (small jaw);
- Bluish sclera (white part of the eye is blue);
- A clinodactyly of the 5th finger (little finger bent towards the others).

The condition can be detected before birth since the growth issue is intrauterine. Infants have a low birth weight and are short in height. As the child ages, the facial features and body asymmetry become more subtle.

Since the severity of the condition varies widely, it can be difficult to make a diagnosis. The diagnosis is essentially clinical and based on a combination of physical characteristics. In addition, in 60% of cases, the genetic test, which reveals abnormalities in methylation (epigenetic change controlling the expression of several genes) of chromosome 7 or 11, can confirm the diagnosis.

MAIN POSSIBLE COMPLICATIONS :

Developmental delay: About 40% of children have delayed motor development caused among other things, by their large head size and weak muscle tone. The same percentage of children are lagging behind in language acquisition. For these children, it is essential to start

treatment quickly (speech therapy, physiotherapy, etc.) in order to support their development. Also, less than 29% of children with Silver-Russell syndrome may have a slight intellectual disability.

Orthopedic issues: When limb asymmetry is significant, limb lengthening surgery can be considered to balance the limb lengths and improve the quality-of-life for clients. However, surgery should only be done at the end of growth. During childhood, suitable orthopedic shoes should be used. In addition, there is a risk of scoliosis and / or kyphosis (hunched back) in about 20% of cases, usually around 8 years of age. Clinical monitoring should be performed regularly during childhood. X-rays will be needed if a problem is suspected. Sometimes surgical fusion is required to correct spinal issues.

Health of the reproductive system: 40% of boys present with cryptorchidism (undescended testis and / or hypospadias (when the urethra is located on the underside of the penis rather than at its end). Cryptorchidism can sometimes resolve on its own, but some boys need surgical intervention. Hypospadias requires surgery, which should be performed by an experienced pediatric surgeon.
A very small number of girls are born with Rokitansky syndrome (total or partial absence of the uterus and the upper part of the vagina).

Advance of puberty: In infants, bone age is delayed but this trend reverses as the child grows if they enter adrenarche, an early stage of sexual development. Usually seen around 8 years of age, puberty starts earlier and progresses faster than expected. This precocious puberty further accelerates the advancement of bone age, which reduces the growth spurt seen during puberty. Therefore, the final height in adulthood is less than initially predicted.
From mid-childhood, therefore, children with Silver-Russell syndrome should see a pediatric endocrinologist to detect the first signs of adrenarche (pre-puberty). If necessary, puberty can be delayed with medication.

Feeding issues: There can be a combination of feeding difficulties and gastrointestinal problems. The feeding issues are mainly linked to oromotor dysfunctions (difficulties in using the lips, tongue and jaw). Gastrointestinal complications include inflammation of the esophagus (esophagitis), gastroesophageal reflux disease (often without visible symptoms), delayed gastric emptying and constipation (more common after the age of 2 years). Some children do not feel hungry during infancy, while others may develop an aversion to food, making it difficult for parents to adequately feed their child. It is suggested to provide less rich, smaller and more frequent meals, and to place babies in an upright position when feeding so that gravity prevents food from returning to the esophagus. Certain medications and dietary supplements can also help. For more severe cases, the placement of a nasogastric tube or a gastrostomy (tube passing through the abdominal wall) may be recommended.

Hypoglycemia: Hypoglycemia occurs in about 20% of cases, usually when the child does not eat for a long time. It therefore often occurs at night. Symptoms of hypoglycemia include

weakness, hunger, dizziness, sweating, and / or headache. It is important to note that children with Silver-Russell syndrome do not always have physical symptoms.
Because of these risks, their urine should be monitored regularly. Indeed, the presence of ketone bodies in the urine is indicative of an upcoming fasting hypoglycemia. If ketone bodies are present, intervention is necessary, as hypoglycemia can develop rapidly and have neurocognitive consequences.

Hypoglycemia is treated according to standard guidelines, including frequent feedings, the use of dietary supplements and complex carbohydrates such as corn starch. To avoid low blood sugar levels, children should never be left without food for long periods of time (even for medical procedures) and should go to the emergency room for a glucose infusion when they are very sick and/or unable to take food by mouth. Learning to measure ketone bodies in your child's urine is helpful for the warning signs of low blood sugar, especially when the child is sick.

Adult Health Problems: Care should be taken to ensure that children eat well, but not too much. Children born with a height and weight well below the average (small for gestational age) as well as a weight gain that is too fast or excessive, are exposed to a higher risk of developing coronary heart disease, hypertension, dyslipidemia (e.g. high cholesterol), and / or insulin resistance or obesity.

Anesthesia: Surgical procedures requiring anesthesia can be a problem as there is a risk of hypothermia and fasting hypoglycemia. An intravenous glucose infusion is therefore almost always necessary. In addition, wound healing may be delayed due to insufficient nutrition. Finally, the irregular arrangement of the teeth and/or the smallness of the jaw can limit access to the upper airways and make intubation difficult. Families should ask to meet with the anesthesiologist before any surgery to ensure that they are aware of the risks [refer to the "anesthesia" factsheet].

TREATMENT:

The management of Silver-Russell syndrome is multidisciplinary (surgery, occupational therapy, orthopedics, physiotherapy, nutritional therapy, gastroenterology, etc.) and preventive, and aims primarily to detect complications and help those affected to have a better quality of life.

In addition, growth hormone therapy should be considered for children with Silver-Russell syndrome since it improves their body composition (especially lean mass), their motor development, and their appetite while reducing the risk of hypoglycemia and optimizing growth. Growth hormone treatment allows the child to add approximately an extra 10 cm (4 in) to their expected final height.

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

- Developmental delay;
- Intellectual disability (if present);
- Orthopedic problems (asymmetry and issues of the spine);
- Early puberty;
- Feeding problems;
- Hypoglycemia.

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=813

NORD – National Organisation for Rare Disorders
https://rarediseases.org/rare-diseases/russell-silver-syndrome/

GARD – Genetic and Rare Disease Information Center
https://rarediseases.info.nih.gov/diseases/4870/silver-russell-syndrome

Association Québécoise des Personnes de Petite Taille

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