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CASE REPORT

Silver-Russell syndrome: case report

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Silver-Russell syndrome, genetics, malnutrition, syndactyly, nutrition disorders, fetal growth retardation.

Abstract

Objective: Silver-Russell syndrome (SRS) is a rare but well-recognized condition associated with classic phenotypic characteristics. This article aims to describe a patient with SRS, in order to help professionals in the diagnosis and adequate therapeutic management, since the early approach results in a better prognosis. **Methods:** This is a case report of a male child, 1 year and 4 months old, admitted to an infirmary, who was diagnosed with SRS. Patient information was collected with the family during hospitalization. Analysis of medical records and literature review was also performed. **Results:** A patient with chronic malnutrition, who had macrocranial physical examination, elongated facies, large ears with low implantation, occipital capillary rarefaction, micrognathia, hypospadias, 5th finger clinodactyly and delayed developmental milestones, received a diagnosis of SRS during hospitalization. Complementary exams ruled out pathologies of the gastrointestinal tract and in the speech-language evaluation, swallowing disorders were not detected. An enteral diet for nutritional recovery was initiated, but the patient maintained insufficient weight gain and an important food aversion, being the patient submitted to gastrostomy. On an outpatient return after hospital discharge, the patient remained low weight gain despite the use of hypercaloric formula and appropriate volume for his age. **Conclusion:** SRS leads to a wide spectrum of abnormal physical characteristics and functional abnormalities. Multidisciplinary monitoring and early, specific intervention are necessary for better management of this group of patients.

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INTRODUCTION

The Silver-Russell Syndrome (SRS) is a rare genetic condition, with a global incidence of 1 to 30/100,000 cases annually, characterized by restricted intrauterine growth, difficulty in postnatal recovery and typical phenotype. The diagnosis is essentially clinical and is based on the Netchine-Harbison scoring system. Such a tool makes it possible to differentiate patients who do not have the syndrome (with 3 or fewer characteristics) and patients who are strongly suspected of it (with 4 or more characteristics). Such features are part of the classic phenotype and include (I) intrauterine growth retardation (length or weight below the 3rd percentile); (II) postnatal growth retardation (height below the 3rd percentile); (III) birth-related macrocrania; (IV) prominent forehead and (V) body asymmetry. In addition, patients with this syndrome may have other common features, such as a triangular face, downward-directed labial commissures, low ear implantation, low muscle mass, irregular teeth, micrognathia, clinodactyly of the 5th finger and excessive sweating[1-4].

Molecular analysis is indicated for patients with a highly suspected clinical syndrome (4 or more characteristics in the score) and helps in the diagnosis by defining subgroups, enabling better management. Despite this, it cannot be used to rule out the clinical diagnosis[1].

60% of the patients with a clinical diagnosis have a genetic basis for SRS. Of these, 30-60% have methylation loss on chromosome 11p15 and 5-10% have maternal uniparental disomy on chromosome 7[5,6].

In the management of the syndrome, nutritional support for weight-height deficit recovery must be included, considering the multifactorial cause such as functional and structural gastrointestinal problems, oro-motor alterations and feeding difficulties with severe food aversion. It is important to note that rapid nutritional recovery increases the incidence of future cardiovascular and metabolic diseases[5,7].

In addition, these patients have proportionally less lean mass in relation to fat mass, especially carriers of the mutation with loss of methylation in chromosome 11p15, when compared to healthy children. This fact makes the BMI targets of the pediatric population high for children with SRS. Therefore, BMI between 11-12kg/m² may be adequate for such patients.

In cases of unsatisfactory enteral nutrition, after ruling out organic causes, enteral nutrition by nasogastric tube or gastrostomy can be considered[1,8-11].

Treatment with growth hormone (GH) should occur after the nutritional approach, and it brings other benefits in addition to linear growth, such as increased appetite, increased lean mass and muscle strength, thus influencing improved mobility. Despite this, it should only be indicated after a well-defined diagnosis, and can be extremely deleterious in other syndromes, such as Bloom's syndrome, increasing the risk of malignancy[10,12,13].

As a consequence of low muscle and liver mass, these children may have hypoglycemic episodes, especially at night, and such episodes may be asymptomatic. The monitoring of hypoglycemia should be done by monitoring ketonuria, evaluating the safe time of fasting. Its prevention can be done with the addition of high molecular weight glucose polymer or raw corn starch to the last meal[14]. Genetic counseling is important because of the risk of familial recurrence[1].

CASE REPORT

Boy, 1-year-and-4-months old, referred to the pediatric gastroenterology outpatient clinic of our service in April 2019, due to chronic malnutrition. In the history, he presented difficulty in latching and sucking since birth, in addition to several unsuccessful attempts to improve weight and height with food supplementation (introduction of infant formula at 1 month of age, food thickener at 6 months of age and food supplement - Fortini® at 8 months). In addition, he presented low acceptance of the food introduction. The patient was born at term, with Apgar scores of 8 and 9, weighing 2,265g and 44cm, small for gestational age and with low birth weight. He had been hospitalized at 1 year and 2 months for treatment of malnutrition, when he started infant formula and was discharged without nutritional recovery. Family history did not reveal comorbidities.

For a better evaluation, the patient was hospitalized at our service in June 2019. Upon physical examination, he had relative macrocrania (head circumference between score -2 and 0), elongated facies, large ears with low implantation, occipital capillary rarefaction, micrognathia, hypospadiae and clinodactyly of the 5th finger. In the nutritional and growth assessment, the patient weighed 5,005g and had a height of 65.5cm, being below the Z score -3 in the height, weight and body mass index (BMI) charts. Upon endocrinological evaluation, there was no deficiency deficit, thyroid alterations or growth hormone deficiency found by screening tests (IGF-1 dosed at 2.8ug/ml – reference value 0.8 to 3.9ug/ml), being indicated outpatient follow-up only. The neurological evaluation showed delay in developmental milestones (he could not stand with support and could not walk), which could be related to low lean mass, and for this reason the patient was referred to the pediatric neurology outpatient clinic for follow-up after nutritional therapy. The speech therapy team ruled out swallowing disorders and maintained oral stimulation during hospitalization in order to facilitate food acceptance.

Total abdominal ultrasound, esophagogastroduodenal seriography, upper digestive endoscopy, transthoracic echocardiography and transfontanelle ultrasound were performed, ruling out anatomical alterations of the gastrointestinal tract, gastroesophageal reflux, swallowing disorder, associated cardiac and central nervous system malformations.

The patient maintained an extremely selective diet, with insufficient food intake for his age, early satiety and low

weight gain, accepting only infant formula, even after several attempts at diet progression with foods varied in flavor and texture.

We decided to start an enteral diet through a nasogastric tube, but despite the sufficient weight gain, there was a worsening of food acceptance. For this reason, gastrostomy was indicated in August 2019, after gastrointestinal disorders were ruled out and severe food aversion was found. After the procedure, infant formula was started and there was a weight gain of 215 grams in 5 days. The patient was discharged after 36 days of hospitalization with diet via gastrostomy, supplemented by infant formula by suction and referred for multidisciplinary outpatient follow-up. On an outpatient follow-up after three months, the patient had low weight gain, despite the use of a hypercaloric formula with adequate volume for age offered by gastrostomy, in addition to low acceptance of oral complementary feeding.

DISCUSSION

The diagnosis of the syndrome is essentially clinical based on classic phenotypic features. According to the Netchine-Harbison score, patients who present at least four of these characteristics will be considered affected by SRS. Although the molecular analysis was not performed on the patient, he had all the phenotypic characteristics; therefore, receiving a clinical diagnosis. According to the literature, molecular analysis helps, but cannot be used for diagnostic exclusion[1,15].

Feeding difficulties with low acceptance and chronic malnutrition were the reason for hospitalization in our case.

Marsaud et al in 2015[5], found in 75 children with SRS, clinical regurgitation or vomiting in 50% of children before 1 year of age and persisted after in 29% of cases and constipation was observed in 20% of patients. Enteral feeding was necessary in 30% of the 75 cases, with gastrostomy in 72% of them (n = 16)[6]. Despite food aversion and difficulty with diet progression both in quantity and quality, the patient in question did not present organic alterations such as constipation, persistent vomiting, anatomical alterations or dysmotility of the gastrointestinal tract. However, severe feeding difficulties and chronic malnutrition made him a candidate for gastrostomy. Invasive intervention was indicated for the patient to receive adequate caloric intake and maintain continuity of nutritional recovery in a home environment. Despite this, the patient returned with unsatisfactory weight gain, corroborating the discrepancy between lean mass and fat mass in patients affected by this syndrome and a BMI below the population average.

Growth hormone (GH) therapy may also be present in the management of SRS, since in addition to linear growth, it benefits these patients by reducing the risk of hypoglycemia, increased appetite, increased lean mass and muscle strength, influencing and thus improving mobility. Despite this, its use in children under 2 years of age requires further studies[1]. Despite all the benefits, it was decided to maintain outpatient endocrinological follow-up and future evaluation of the use of such therapy, since the patient was still undergoing an approach for nutritional recovery and had no episodes of hypoglycemia.

CONCLUSION

Patients with SRS needs a multidisciplinary outpatient follow-up so that the necessary interventions are carried out, in search of a favorable evolution and a better clinical and nutritional prognosis. In the case previously reported, even after nutritional intervention with gastrostomy and introduction of a hypercaloric diet, there was no satisfactory weight gain for age. Due to the multifactorial basis associated with low weight gain, we concluded that several of the factors associated with the syndrome interfere with nutritional evolution and recovery, and not only the inadequacy of energy balance due to reduced caloric intake. Thus, the indication of gastrostomy must be considered since the adequate protein-calorie supply will not always achieve the objective of nutritional recovery.

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