Revista Odontológica Mexicana
Órgano Oficial de la Facultad de Odontología UNAM

Clinical case

Orofacial Development and Craniofacial Manifestations of Silver-Russell Syndrome: Case Report

Daiana Cristina Pereira-Santana[1], Daniel Maurício Meza-Lasso[2], Luís Cláudio Cardoso-Santos[2], Eduardo Francisco de Deus-Borges[2], Roberto Almeida-de Azevedo[2]

1. Universidade Federal da Bahia, Faculdade de Odontologia, Departamento de Cirurgia e Traumatologia Bucomaxilofacial/ Departamento de Pós-Graduação em Odontologia e Saúde. Salvador, Brasil.
2. Universidade Federal da Bahia, Faculdade de Odontologia, Departamento de Cirurgia e Traumatologia Bucomaxilofacial. Salvador, Brasil.

Corresponding author:
Daiana Cristina Pereira Santana
E-mail: doutoradaianabucomaxilo@hotmail.com

Received: June 2021
Accepted: September 2022

Cite as:
Pereira-Santana DC, Meza-Lasso DM, Cardoso-Santos LC, de Deus-Borges EF, Almeida-de Azevedo R. Desarrollo orofacial y manifestaciones craneofaciales del síndrome de Silver-Russell: Presentación de caso. [Orofacial Development and Craniofacial Manifestations of Silver-Russell Syndrome: Case Report]. *Rev Odont Mex*. 2022; 26(4): 39-44. DOI: 10.22201/fo.1870199xp.2022.26.4.79743

Abstract

Introduction: Silver-Russell syndrome is a heterogeneous disease in its clinical and genetic manifestations, feature prenatal and postnatal growth restriction, relative macrocephaly, body asymmetry and some typical facial characteristics that mainly include a small and triangular face, large mouth and inverted lip corners, prominent forehead, normal head circumference and micrognathism. **Objective:** To detail the craniofacial findings through the case presentation of a patient with the referred syndrome, attended by the Centrinho das Obras Sociais Irmã Dulce, in

Salvador, Bahia, Brazil, with the purpose of guiding the dentist in relation to the diagnosis and possible therapeutic conducts. **Case presentation:** An eight-year-old female patient, diagnosed with Silver-Russell syndrome, who presented low birth weight and difficulty gaining weight since childhood. She presented the classic facial characteristics of the syndrome (triangular face, micrognathia, prominent frontal region, inverted lip commissures), in addition to the presence of cleft palate, a rare characteristic in the syndrome. The patient was scheduled for surgery to rehabilitate the cleft in the palate (after stipulated weight gain) and complementary ortho surgical support. **Conclusions:** in the scientific dental literature, there are few works that address the topic. We emphasise the need for early monitoring of these patients in order to identify, prevent and correct the manifestations caused by the syndrome.

Keywords: Silver-Russell Syndrome, genomic imprinting, craniofacial anomalies.

INTRODUCTION

Silver-Russell syndrome was described in the 50s by two researchers independently. In 1953 Silver *et al*. described two patients with intrauterine and postpartum growth retardation, short stature, hemihypertrophy, high levels of urinary gonadotropins and abnormal psychomotor development[1]. In 1954, Russell reported the existence of five congeners infantile patients, with pre- and post-natal growth failures, with disproportionately short upper limbs, clinodactyly of the fifth finger and characteristic facial pattern (triangular face, prominent forehead, small jaw, thin lips with inverted lip corners downwards), only two of them being physically asymmetrical[2].

Currently, it is known that it is a heterogeneous disease in its clinical and genetic manifestations, where prenatal and postnatal growth restriction, relative macrocephaly, body asymmetry and some typical facial characteristics are observed. It is characterised as one of the genomic imprinting disorders, which results as a consequence of incorrect genetic expressions. Maternal uniparental disomy of chromosome 7 is responsible for 10% of cases of Silver-Russell syndrome, and about 50% of patients manifest hypomethylation in telomeric imprinting control region 1 on chromosome segment 11p15.5, leaving about 40% of cases with unknown aetiologies[3]. An incidence of 1:300,000 live births is estimated, affecting men and women equally, and around 19% of cases usually present more than one case within the family, favouring evidence of genetic causes[4,5].

Within the picture of craniomaxillofacial abnormalities, a small and triangular face is current, with a large mouth and inverted lip corners, a prominent forehead, a normal head circumference and micrognathism, representing a characteristic profile. Hypoplasia of the middle third of the face is highlighted, thin lips, delayed dental eruption, missing teeth, fissured tongue, reduced condyles, facial lipodystrophy, deep-set eyes, blue sclera, long eyelashes, large and round nose, underdeveloped nasal alae, broad columella, anteverted nares, short nose, fine hair. Likewise, the mandibular arch is often narrow, with crowding and lingualization of the mandibular incisors. Micrognathia results in small chin and anterior crossbite. These children have notable facial asymmetry. They may have either an anterior and posterior crossbite or a scissor bite, which impairs chewing. Velopharyngeal insufficiency with or without submucosal fissure can occur in patients with the syndrome with hypomethylation of chromosome 11p15. In addition, young children present otitis media[5-11].

The surgical treatment used for craniomaxillofacial alterations will depend on the type of manifestation and its relationship with aesthetic and functional issues, since not all patients present the same phenotype.

CLINICAL CASE PRESENTATION

An eight-year-old female patient, with Silver-Russell syndrome, born at 38 weeks of gestation, with low weight (1.225 kg). She remained hospitalized for three months to gain weight, so supplementary feeding (NAN®, Nestlé S.A, Vevey, Switzerland) was necessary in addition to breast milk and she was only discharged from the hospital when she reached 1.850 kg in weight. In June 2014, she was hospitalized for nutritional support and weight gain, while corrective surgery for the cleft palate was planned, a period in which the diagnosis of the syndrome was confirmed. Since then, the patient's mother has reported difficulties gaining weight, despite a proportional and age-appropriate diet. During the current physical examination, short stature and low weight, slight asymmetry in the chest, with the right nipple higher than the left and preserved expandability, clinodactyly in the fifth finger, asymmetry in relation to the size of the hands and upper limbs were identified. The patient does not have neurological and/or psychomotor deficits, however, she does have phonation difficulties, with hypernazalized speech in response to velopharyngeal insufficiency. She was under treatment with pancreatic enzyme 10,000 IU as indicated by the attending endocrinologist. Maxillofacial physical examination showed a disproportion of the facial thirds, with a prominent forehead and triangular face, low implantation of the ears, voluminous nose, good mouth opening, presence of complete post-foramen cleft palate, anterior and posterior crossbite, dental agenesis, ogival palate, and good oral hygiene (Figure 1. A-E). Considering the family history, it is suspected that the patient's older sister has several conditions of the same syndrome and is undergoing analysis awaiting diagnosis. The patient is being scheduled for corrective surgery for the cleft palate, in order to regain the necessary weight. Clinical-orthodontic support will be proposed to treat maxillary atresia.

DISCUSSION

Treatment aimed at maxillofacial deformities in patients with Silver-Russell syndrome must be approached by a multidisciplinary team with an orthodontist, maxillofacial surgeon, plastic surgeon, speech-language pathologist and otorhinolaryngologist.

The correction of the cleft palate has as its purpose, among other aspects, the good development of phonation, considering some protocols described in the literature. The Marburg's Protocol (Germany) establishes closure of the soft palate at six months of age and the hard palate no earlier than 13 years of age. Likewise, Malek's operative protocol anticipates closure of the soft palate to allow speech without compensatory mechanisms and postpones closure of the hard palate to minimize the effects of iatrogenesis on the face[12]. In our case, the patient had to postpone the palate closure surgery, due to low weight and malnutrition, to fit into the appropriate age phase for surgery. Postponing surgery was the most indicated option considering the risk-benefit, and the decision was supported in the literature by the study by Canada *et al*., where they showed that preoperative malnutrition can be a factor for postoperative complications and, therefore, expose the patient to a longer hospitalization time[13].

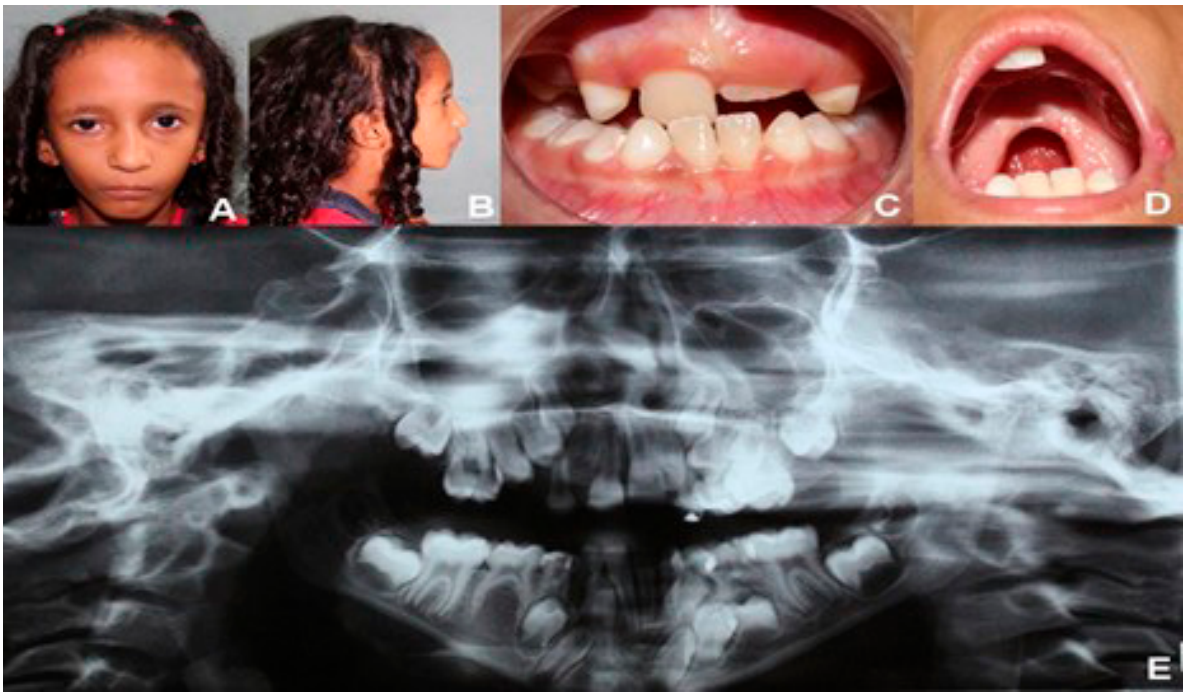

Figure 1. Photographs of the clinical case. A. Frontal view showing triangular face, with disproportion between the facial thirds and micrognathia. B. Lateral view: prominent forehead and low implantation of the ears. C. Frontal occlusal view: anterior and posterior crossbite, agenesis and delay in tooth eruption. D. Intraoral view: Presence of complete post-foramen cleft palate. E. Orthopantomography showing delayed tooth eruption, impaction and agenesis.

Bergman *et al*. developed a study with the objective of describing craniofacial morphology, occlusion and dental age in infants with Silver-Russell syndrome, in which sixteen participants of both sexes were included. From radiographs, facial and dental maturation measurements were determined, and plaster models were needed for analysis of biometric measurements. The authors observed that the majority of infants affected by the syndrome presented smaller linear dimensions of the face, as well as irregularities in facial proportions, for example, a small maxilla, a retrognathous and inclined mandible, proportionally greater anterior facial height compared to the posterior facial height. The frequency of malocclusions was greater and the height of the palate showed a trend to increase. Tooth maturation was within normal limits, while tooth eruption time was slightly delayed. From these data, they concluded that the higher percentage of malocclusions in infants with Silver-Russell syndrome may lead to a greater need for orthodontic treatment[9]. Based on these data, our patient began orthodontic treatment for bimaxillary atresia, agenesis and delayed tooth eruption, in an attempt to improve the course of the pre-existing dentofacial deformity.

Within the possible classic findings described in the syndrome, a consensus was published by Wakeling *et al*. in 2016, with clinical-surgical recommendations for each type of region, organ or system compromised by the syndrome. Regarding the maxillofacial region, they discuss that orthodontic intervention in infants with the syndrome can help normalise oropharyngeal function and facial appearance and that multiple orthodontic techniques are used successfully[7]. Now, surgically assisted rapid palatal expansion is the most effective technique to modify the facial pattern of the face.

In relation to orthodontic issues, the same authors[7] report that many patients with Silver-Russell syndrome report excessive daytime fatigue, snoring and/or interrupted sleep, which may suggest the presence of Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS). Data are still very limited in relation to sleep problems and more studies are necessary[7]. Sleep-related problems were not described by our patient's mother; however, due to the atresia of the articular bones, the subsequent development of this type of alteration cannot be ruled out. No early surgical intervention was introduced; however, in the future, orthognathic surgery with advancement of the mandible may be a complementary option to the treatment, if the problem manifests itself.

Regarding pre- and post-surgical considerations for patients with Silver-Russell syndrome, the literature is not specific when it comes to surgeries exclusive to the maxillofacial complex. It is very important that, apart from the adequate pre-operative nutritional regimen mentioned above, care inherent to the particular characteristics of each patient must be taken into consideration by surgeons and anaesthesiologists. Which include, on the one hand, airway difficulty attributed to micrognathia, a complicating factor for endotracheal intubation commonly associated with some craniofacial syndromes[14], and on the other, poor tooth position in the dental arches. Jointly, other risks that are also associated with the syndrome and may be common should be prevented, such as episodes of hypoglycaemia[15], hypothermia due to short stature, low body mass index, and increased head size.

CONCLUSIONS

Although the literature lacks specific studies of the craniofacial manifestations of Silver-Russell syndrome, as well as in the dental management of patients, it is important to explain such cases based on clinical experience. The scarcity of works focused on dentistry and the phenotypic variability of the syndrome mean that the course and extent of maxillofacial problems still remain unpredictable. With this, we emphasise the need for early follow-up by the maxillofacial surgeon in order to identify and prevent further damage, and also correct the manifestations found so far.

BLIBLIOGRAPHIC REFERENCES

1. Silver HK, Kiyasu W, George J, Deamer WC. Syndrome of congenital hemihypertrophy, shortness of stature, and elevated urinary gonadotropins. *Pediatrics*. 1953; 12(4): 368-376.
2. Russell A. A syndrome of "intra-uterine" dwarfism recognizable at birth with craniofacial dysostosis, disproportionately short arms and other anomalies (5 examples). *Proc R Soc Med*. 1954; 47(12):1040-1044.
3. Ishida M. New developments in Silver–Russell syndrome & implications for clinical practice. *Epigenomics*. 2016; 8(4): 563–580. DOI: 10.2217/epi-2015-0010
4. McNamara GI, Davis BA, Dwyer DM, John RM, Isles AR. Behavioural abnormalities in a novel mouse model for Silver- Russell Syndrome. *Hum Mol Genet*. 2016; 25(24): 5407-5417. DOI: 10.1093/hmg/ddw357
5. Shah S, Kaur M, Chandran JPV, Sekhar K S, Vijay VK, Babaji P. Silver-Russel Syndrome (SRS): A review of current concepts. *IOSR J Pharm*. 2013; 3(8): 22-26. DOI: 10.9790/3013-0381022-26

6. Pinto F, Martins JR, Soares P, Mota C. Síndroma de Silver-Russel. Um Caso Clínico. *Acta Pediatr Port.* 1999; 30(5): 421-423. https://ojs.pjp.spp.pt/article/view/5513/4278
7. Wakeling EL, Brioude F, Lokulo-Sodipe O, O'Connell SM, Salem J, Bliek J, *et al*. Diagnosis and management of Silver–Russell syndrome: first international consensus statement. *Nat Rev Endocrinol*. 2017; 13(2): 105–124. DOI: 10.1038/nrendo.2016.138
8. Rodrigues LST, Francisco CCSSM, Coutinho TCL. Síndrome de Silver-Russell: relato de caso clínico. *Revista Fluminense de Odontologia*. 2010; 16(34): 17-20. DOI: 10.22409/ijosd.v2i34.88
9. Bergman A, Kjellberg H, Dahlgren J. Craniofacial morphology and dental age in children with Silver–Russell syndrome. *Orthod Craniofac Res*. 2003; 6(1): 54-62. DOI: 10.1046/j.1439-0280.2003.2c209.x
10. Cullen CL, Wesley RK. Russell–Silver syndrome: microdontia and other pertinent oral findings. *ASDC J Dent Child*. 1987; 54(3): 201–204. PMID: 3473100
11. Hodge, N, Evans CA, Simmons KE, Fadavi S, Viana G. Occlusal characteristics of individuals with growth hormone deficiency, idiopathic short stature, and Russell–Silver syndrome. *J Dent Child (Chic.)*. 2015; 82(3): 135-140. https://www.ingentaconnect.com/content/aapd/jodc/2015/00000082/00000003/art00003
12. Miachon MD, Leme PLS. Tratamento operatório das fendas labiais. *Rev Col Bras Cir.* 2014; 41(3): 208-215. DOI: 10.1590/s0100-69912014000300013
13. Canada NL, Mullins L, Pearo B, Spoede E. Optimizing perioperative nutrition in pediatric populations. *Nutr Clin Pract*. 2016; 31(1): 49-58. DOI: 10.1177/0884533615622639
14. Huang AS, Rutland L, Hajduk J, Jagannathan N. Difficult airway management of children in ambulatory anesthesia: challenges and solutions. *Ambulatory Anesthesia*. 2016; 3: 37–45. DOI: 10.2147/AA.S91983
15. Garcia PF, Salvador KK, Moraes TFD, Feniman MR, Crenitte PAP. Processamento auditivo, leitura e escrita na síndrome de Silver-Russell: relato de caso. *Rev. soc. bras. fonoaudiol*. 2012; 17(1):101-105. DOI: 10.1590/S1516-80342012000100018