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CRI DU CHAT SYNDROME, DENTAL CHARACTERISTICS: CLINICAL CASE REPORT

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Gleiciane Oliveira de Souza[1], Israel Cardoso Caldeira[2], Kamila Nascimento Breda[3], Kesia Zamerim Santana[4] and Daniela Pertel Milleri[5].

ABSTRACT

Cri Du Chat Syndrome is characterized by anomalies that alter the physical and sensory structures of the body, as well as the facial anatomy, affecting everything from the dental structure to oral functions. The dental management of this type of patient is complex. From this analysis, it is possible to identify the particularities of dental treatment in these patients, considering their specific needs and aiming at their quality of life. After understanding the relationships between the syndrome and dental care, it is possible to individualize, improve, and optimize the oral health of patients with this genetic condition. This study aimed to report the dental characteristics associated with Cri Du Chat Syndrome, addressing both its craniofacial characteristics and the implications for dental care. The study was based on the case of a 29-year-old female patient diagnosed with this syndrome, who was treated at the dental clinic of the Multivix University Center, in Vitória, Espírito Santo.

Keywords: Cri Du Chat Syndrome. Dental Characteristics. Craniofacial Development. Patients with Special Needs.

[1] Academics of the Dentistry course at Centro Universitário Multivix Vitória
[2] Academics of the Dentistry course at Centro Universitário Multivix Vitória
[3] Academics of the Dentistry course at Centro Universitário Multivix Vitória
[4] Academics of the Dentistry course at Centro Universitário Multivix Vitória
[5] Master in Dental Clinic - Multivix Teacher - Vitória

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INTRODUCTION

In the health sciences, the genetic syndrome is understood as a clinical condition resulting from changes in the genetic material of an individual, either by modifications in the number, structure or function of chromosomes, or by mutations in specific genes (Schaefer; Thompson Jr., 2014).

The changes can occur spontaneously or be inherited from one of the parents, and often result in a characteristic set of signs and symptoms that can affect several areas of development and physiology (Ikehara, 2011).

Such phenotypic alterations range from congenital malformations to alterations or impairments in physical and cognitive development, whose characteristics are determined by the nature of the mutation and the extent of the genetic impact, and may vary significantly among affected individuals, directly influencing the quality and life expectancy of patients (Schaefer; Thompson Jr., 2014).

"Although Cri Du Chat is considered a rare disorder, it is one of the most common chromosomal abnormalities. The incidence ranges from 1 in 15,000 to 1 in 50,000 live births" (Ajitkumar; Jamil; Mathai, 2022).

Cri Du Chat Syndrome is a disease considered rare, as it affects few people in the world population, however it stands out as the most common among the autosomal syndromes that affect humans.

The definitive diagnosis of the disease is made through genetic testing, but the physical characteristics that patients with this syndrome present are visible in the first years of life, allowing early detection, and consequently implementing immediate intervention measures in order to improve their quality of life (Ajitkumar; Jamil; Mathai, 2022).

Although considered a rare and uncommon genetic disease, especially in clinical dental practice, Cri Du Chat Syndrome presents orofacial manifestations that require a specialized therapeutic approach.

The relevance of this syndrome for the dental surgeon lies in the knowledge of the stomatognathic and craniofacial characteristics of the patient with it, in order to carry out, in addition to the correct management and referral of the case, the establishment of possible advances in terms of dental diagnosis (Rentería *et al.*, 2020).

According to Heras (2017), the dental management of patients with Cri Du Chat Syndrome can be difficult, due to the medications they use and the problems related to mental disability.

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In view of this, it is important that dental surgeons have a minimum understanding of the peculiarities, both in the behavior and development of children with this condition, for the success of therapy in these patients.

Being a rare condition, as already mentioned, many professionals neglect the treatment of these patients, or even refuse to provide care due to lack of knowledge about this condition (Corcuera-Flores *et al.*, 2016).

Knowing and understanding the particularities of these patients allows the health professional, as well as the dental surgeon, to detect early and fulfill their role and moral obligation to offer a dignified, adequate treatment that improves the quality of life of these individuals. Rentería *et al.* (2020), states that for the dental consultation of syndromic patients to be well managed, the professional needs to know their craniofacial and stomatological characteristics.

Although the patient with Cri Du Chat Syndrome has characteristics that are of interest in the dental field, the scientific literature is scarce regarding studies and published studies that involve dental approaches, management and techniques to care for these patients. In view of this, Zaragoz (2021) points out that, although the syndrome is considered rare, it is important to study and investigate more cases of the disease.

It is important to highlight the difficulty of those responsible for the patient in maintaining dental activities, such as oral hygiene at home. Taking into account the physical and motor disabilities of the patient, and even of those responsible for performing maintenance with precision, the presence of the dental surgeon in the lives of these patients is extremely important. To this end, it is necessary for these professionals to know about the Syndrome in order to better serve them.

Therefore, the objective of this study is to report a clinical case of a 29-year-old female patient with Cri Du Chat Syndrome, identifying her clinical characteristics, as well as the dental approach addressed.

THEORETICAL FRAMEWORK

CRI DU CHAT SYNDROME

Discovered by Dr. Lejeune in 1963, Cri Du Chat Syndrome is also known as "Cat Meow Cry" due to one of its main and most striking clinical characteristic, manifested in the first years of life, which is that the child's cry is similar to a cat's meow (Zaragoza, 2021).

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Crying similar to a cat's meow is considered a characteristic finding in the neonatal period, however it is not considered pathognomonic of the syndrome. It is of high volume, monochromatic, that is, with vibrations at the same frequency, and which disappears as age advances, making the diagnosis of the syndrome more difficult. In cases where the diagnosis is delayed, the signs and symptoms are less specific and milder, which can cause confusion in the diagnosis with other diseases with similar neurological alterations (Ribeiro *et al.*, 2020).

Cri Du Chat Syndrome is an autosomal genetic disorder caused by the partial or total deletion of the short arm of chromosome 5 (5p-). This alteration is present between the 5p14 and 5p15 regions, and usually the alterations corresponding to the 5p15.33 region are related to the presence of a cat's meow-like cry. The exclusion of each piece of the chromosome, that is, of a piece of genetic material in the short arm, can trigger a specific peculiarity of the syndrome, such as the alteration present in the 5p15 region.31 is associated with microcephaly in patients with Cru Du Chat Syndrome (Heras, 2017; Rentería *et al.*, 2020).

According to Ajitkumar, Jamil, and Mathai (2022), the deleted region of the chromosome and the fact that it is partial or total, will influence the clinical condition of the patient with the syndrome, as well as the severity and progression of the pathology. This means that changes in the individual's phenotype are attributable to changes in genotype. Therefore, it characteristically presents with different facial particularities, intellectual disability, and developmental deficit.

Zaragoza (2021) reiterates that although the genotype-phenotype correlation is not fully established, the syndrome has a variable spectrum in terms of its clinical characteristics and severity, which seem to depend on the genetic content and size of the deletion.

With regard to the incidence of the syndrome, it can vary from 1 in 15,000 to 1 in 50,000 live births, although the exact incidence and prevalence of the disease in the world have not yet been established, nor between races, in the same way that the specific risk factors related to prenatal events or the age of the parents are not yet clear. However, there are some reports in the literature that indicate parental exposure to radiation, toxemia, hyperemesis and anorexia (Ajitkumar; Jamil; Mathai, 2022).

According to Rentería *et al.* (2020), Cri Du Chat Syndrome is more prevalent in females, although between 10 and 15% of the cases described in the literature, it was

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analyzed that at least one of the parents had a similar chromosomal genetic alteration. In addition, the life expectancy of individuals with the syndrome is long, and in some cases exceeds 60 years of age. Mortality rates are close to 10% in the first year of life, with the main causes being cardiac or asphyxiating.

According to Heras (2017), the prognosis of patients with Cri Du Chat Syndrome has a notable influence on the type of chromosomal deletion, as well as its size and location, since it is directly related to the severity of alterations such as psychomotor and mental regression.

Therefore, it is understood that early diagnosis is the main way to improve the prognosis of individuals, as it allows the establishment of therapeutic, preventive methods that promote the psychic and physical development of patients.

Among the methods to improve the prognosis are the performance of surgical interventions that are necessary, the establishment of integration of patients in rehabilitation programs, the introduction of healthy routines that stimulate conversation (Heras, 2017).

DIAGNOSIS AND CHARACTERISTICS OF THE SYNDROME

The diagnosis of Cri Du Chat Syndrome can be made early in an ultrasound exam while still in the prenatal phase, taking into account characteristics such as cerebellar hypoplasia, followed by cardiac abnormalities, fetal hydrops/fluid collection, ventriculomegaly, choroid plexus cyst, and nasal bone hypoplasia (Traisrisilp et al, 2022).

However, the confirmation of the diagnosis requires clinical screening in which the disease can be suspected from its atypical manifestations, and through the analysis of the chromosomal karyotype where questionable fragments of genetic exclusion can be found, which in addition to helping in the diagnosis, can help in the prognosis of the syndrome (Bai *et al.,* 2022).

According to Pereira *et al.* (2013), a cat's meow-like cry can be explained by the abnormal development of the larynx, that is, laryngeal hypoplasia, which in the first years of life produces changes in language and high-pitched voice in the child and becomes less evident during adolescence.

Among the most striking craniofacial features is microcephaly, a condition in which the skull is smaller than normal, reflecting incomplete brain development (Bai *et al.,* 2022). Microcephaly contributes to the round and diminutive shape of the head, which is common

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in these patients, also impacting brain volume and cognitive development (Corcuera-Flores, 2016).

In addition, carriers usually have a round face and, in some cases, slightly asymmetrical, with eyes well separated (hypertelorism), which accentuates the characteristic appearance of the syndrome (Corcuera-Flores, 2016).

Also noteworthy in the clinical characteristics of the patients are cat-like crying in childhood, microcephaly, developmental delay and severe mental retardation, rounded face, hypotropia, wide eye space, low ear position, epicanthus, hypotropia of the cleft eye, penetrating hand, among other characteristics (Bai *et al.,* 2022).

Rentería *et al.*, (2020), describe in their studies a list of craniofacial alterations in patients with Cri Du Chat Syndrome, listing as the most prevalent: alterations in the nasal region, epicanthus, retrognathism, microretrognathism, hypertelorism, round face, facial dimorphism, and microcephaly. They also include the following stomatological alterations: high or elevated palate, muscle hypotonia of the perioral region, open bite, short nasolabial philtrum, malocclusion, and laryngeal hypoplasia.

Pereira *et al*., (2013) also report as orofacial alterations present in Cri Du Chat Syndrome, high and accentuated palate, malocclusion, mandibular microretrognathia, poor oral hygiene, delayed tooth eruption, chronic generalized periodontitis and enamel hypoplasia.

Another relevant aspect is the respiratory and eating problems common in patients with Cri du Chat syndrome, which can lead to predominantly mouth breathing. Mouth breathing contributes to the dryness of the oral mucosa and reduces the effectiveness of saliva, which has protective functions, such as dental remineralization and antibacterial action (Rodriguez-Caballero, 2010; Molina- Garcia, 2016).

These conditions increase the risk of developing oral caries and infections, carious lesion and periodontal disease in patients with this condition, and may be related to orofacial changes and poor oral hygiene, resulting from difficulty in opening the mouth (Molina-Garcia et al., 2016).

In their systematic review, Corcuera-Flores *et al*., (2016) mentioned that of seven selected studies, two focused on the orofacial characteristics of individuals with the Syndrome, and these characteristics, listed in order from the most to the least common, were found in people with this condition (Table 1).

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Table 1: Oral and perioral alterations in patients with Cri Du Chat Syndrome

Less common characteristics	Most frequent characteristics	Most common characteristics
Macroglossias	High palate	Retrognatismo mandibular
Dental opacities	Macrodontia and macrostomy	Anterior open bite
Enamel hypoplasia		Angle class II malocclusion
Dental agenesis		Hypotonic perioral muscles
Root resorption		
Dental transposition		
Supernumerary teeth		
Temporomandibular joint disorders		

Source: Corcuera-Flores *et al*., 2016 (Adapted by the authors).

Therefore, it can be considered that the implications of these conditions for the oral health of patients require a preventive and multidisciplinary approach, which considers the anatomical and functional particularities of these individuals. It is essential that dental follow-up is started from childhood, with specific guidelines for oral hygiene and early orthodontic interventions that can improve the function and aesthetics of the oral cavity.

DENTAL TREATMENT AND APPROACH

Taking into account the impossibility of recovering the lost genetic material, and that the consequences of the disease involve intellectual and physical capacities from the first years of life, as already mentioned, it is of paramount importance to monitor these patients in a multidisciplinary way in order to improve their quality of life, as well as that of their families (Rentería *et al.*, 2020).

Patients with Special Needs (PNE) often face motor limitations due to their conditions, as well as difficulties in cooperation and aggressive reactions, which ends up impairing their oral hygiene, even when there is someone responsible for their supervision (Barros, 2024).

These patients usually have prevalent and more common oral alterations, such as dental caries and periodontal disease (Veríssimo; Azevedo; Rego, 2013).

In view of this, when understanding the absence of a possible curative treatment of the disease, it is essential and incumbent on health professionals, such as the dental surgeon, to focus the care and treatment of these patients on the alterations manifested by the syndrome according to each particular case.

Although the literature is scarce with regard to clinical evaluations necessary during childhood, adolescence and adulthood to identify the complications of the disease early, Liverani *et al.* (2019) discussed in their study, in a generic way, recommendations for the clinical dental management of patients with Cri Du Chat Syndrome.

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During childhood, the presence of malocclusion is common, requiring early orthodontic evaluation, as it can interfere with the patient's swallowing and breathing, consequently leading to worsening sleep quality. The presence of carious lesions due to atypical chewing and food debris in the mouth can cause pain to the patient, even if the child does not know how to locate it, and become the cause of more serious infections. Therefore, the authors suggest that the first dental evaluation should take place at 12 months of age, followed by regular annual check-ups (Liverani *et al.*, 2019).

For the treatment of children with Cri Du Chat Syndrome who have obstructive sleep apnea, skeletal expansion combined with tissue reduction allows mandibular advancement, in order to improve the child's facial profile and enable its decannulation (Heras, 2017).

Bermúdez *et al.* (2021) mentions that children with Cri Du Chat Syndrome have unsociable behaviors, common problems of aggressiveness, uncontrolled movements, and hyperactivity, which makes it difficult to manage this patient.

According to Pereira *et al.* (2013), dental treatment, whenever possible, should be performed under local anesthesia and, if necessary, use the aid of sedatives to improve the patient's cooperation, thus avoiding injuries. Once general anesthesia is necessary, it should be done with caution and using the necessary measures, as it can increase the risk of complications, in addition to the fact that retrognathia and the deep palate can make intubation difficult.

In agreement, Rentería *et al.* (2020), attest that in situations where the patient is not a collaborator and it is necessary to perform surgical procedures, the presence of changes in the patient's larynx and the difficulty of performing intubation should be considered, so it may be necessary to use anesthetic alternatives.

The same authors also clarify the fundamental and constant dental follow-up of these patients, through preventive procedures such as guidance on appropriate oral hygiene techniques, correction of inadequate dental positioning through interceptive orthodontics, surgical treatments, among others (Rentería *et al.*, 2020).

Bermúdez *et al.* (2021) reiterates that dental treatments should be complemented with the help of therapy aimed at physical and motor rehabilitation, visual and auditory stimuli, to stimulate and improve the attention, communication, and visualization of patients with the syndrome. In addition, therapy in conjunction with the adaptations of the social and family sphere in which the child is developing, will help control sleep disorders and hyperactivity, characteristics frequently reported in patients with Cri Du Chat Syndrome.

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Pereira *et al.* (2013) elucidates that the fact that the patient has Cri Du Chat Syndrome is not an impediment to undergoing dental treatment on the patient. After the evaluation, it is enough to make a complete explanation about the treatment conduct and approach to the guardians and the child, in order to subtract expectations and generate confidence in the procedure, and the patient collaborates with the treatment.

In view of the above, it can be stated that they require a multidisciplinary treatment and that sometimes their management becomes complex and challenging. Therefore, it is extremely important that dental surgeons know the disease in order to promote quality oral and general health to the patient.

The rehabilitation of these patients should continue throughout their lives, since a favorable evolution can be obtained at more advanced ages (Bermúdez, *et al.*, 2021).

RESULTS AND DISCUSSION

This study was approved by the Ethics Committee and has CAAE (Certificate of Presentation of Ethical Appreciation) No. 84370024.9.0000.5066.

A 29-year-old female patient attended the Dental Clinic of the Multivix University Center – Vitória ES, accompanied by her guardian, seeking dental treatment, with the main complaint of "gingival bleeding".

In the anamnesis, the mother reported that the patient had Cri Du Chat Syndrome, also known as "Cat's Meow Cry", presenting a quadriplegia-type physical disability, with severe neuropsychomotor development delay, microcephaly and severe intellectual disability (Figure 1).

Figure 1 – Physical characteristics of the patient

Source: The authors

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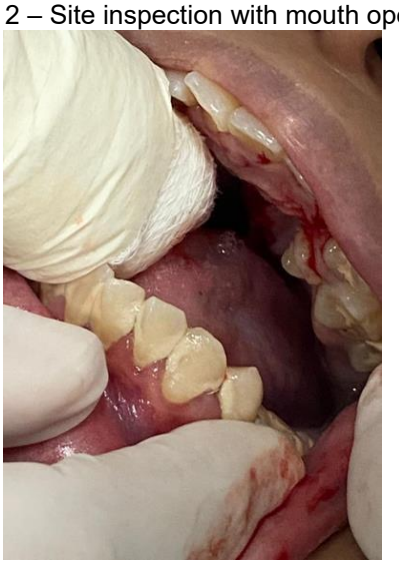
The patient's extraoral clinical examination showed characteristics pertinent to the syndrome according to the literature. The presence of mandibular retrognathism, epicanthus, hypertelorism, round face, dimorphism, and microcephaly was noted.

The patient was resistant and reluctant, and local inspection was possible only under protective stabilization and with the use of mouth openers (Figure 2) (Table 2).

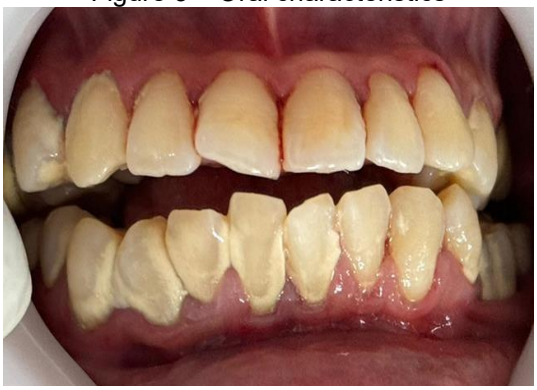
Figure 2 – Site inspection with mouth openers



Source: The authors

At the initial intraoral clinical examination, the presence of permanent dentures was observed, with the absence of element 47 and third molars, elements 14 and 24 in dental transposition; generalized biofilm; absence of carious lesions; bleeding gums to the touch in addition to generalized supragingival calculi in both upper and lower arches; malocclusion of the anterior open bite and unilateral posterior cross bite; in addition to the presence of sialorrhea In the incisal region of elements 11, 12, 21 and 22, an image suggestive of enamel hypoplasia was observed (Figures 3 to 5).

Figure 3 – Oral characteristics



Source: The authors Figures 4 and 5 – Oral characteristics

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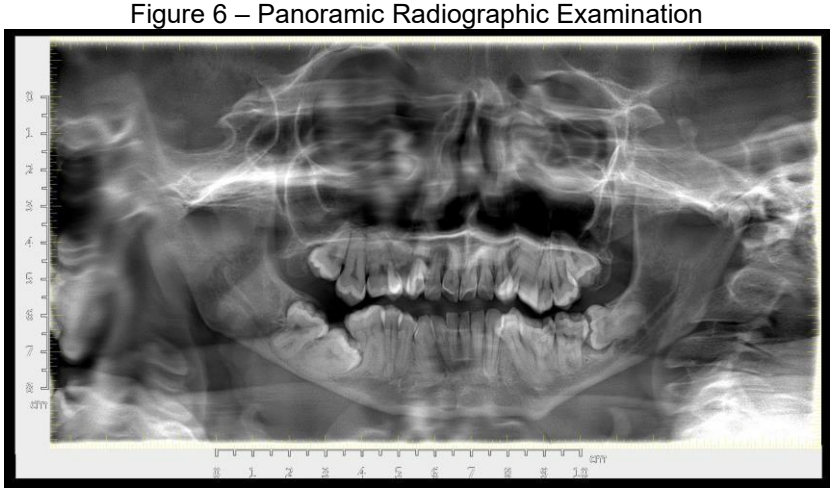
Figures 4 and 5 – Oral characteristics

Source: The authors

A panoramic radiographic examination was requested as a diagnostic complement, and after analysis, the appearance of dental crowding of elements 14/15, 24/25 and 34/35 was observed; intimate relationship of the crown of element 47 with the cervical (distal surface) of element 46; elements 18, 28 and 48 impacted vertically; element 38 impacted in a horizontal position; element 47 impacted in angled mesium position. (Figure 6) (Table 2).

Figure 6 – Panoramic Radiographic Examination



Source: The authors

Table 2: Patient's oral and perioral changes

Less common characteristics	Most frequent characteristics	Most common characteristics
Enamel hypoplasia	Periodontitis crônica Generalized	Retrognatismo mandibular
Dental transposition	Dimorphism	Anterior open bite
Epicanto		Class II malocclusion of Angle
		Hypertelorism
		Microcephaly
		Round Face

Source: The authors

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As a therapeutic conduct, the person in charge was proposed: oral hygiene guidance with plaque control; periodontal therapy with ultrasound scaling and root planing, organized in short sessions, with fortnightly intervals, due to the patient's difficulty in moving to the institution (Figures 7 to 10).

Figures 7 and 8 – Initial appearance before the therapeutic approach

Source: The authors

Figures 9 and 10 – Image right after the first periodontal scaling session

Source: The authors

Due to the patient's intellectual disability and in order to limit involuntary movements and promote safe and less traumatic care, the use of protective stabilization was necessary during all consultations, with the help of a team composed of three students and three professors from the school clinic, plus the support of the person in charge, who previously signed the Informed Consent Form.

After two months of treatment, favorable results were obtained, with oral hygiene instructions and dietary counseling reinforced for the patient's legal guardian, advising her of the indispensability of returning for subsequent follow-up every six months (Figures 11 to 13).

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Figures 11 to 13 – Immediate post-treatment result

Source: The authors

FINAL CONSIDERATIONS / CONCLUSIONS

In view of the above, the importance of studies on Cri Du Chat Syndrome in the field of dentistry is evident, due to the scarcity of information regarding this pathology and dental findings, given the wide and complex range of characteristics that this condition presents, as well as the craniofacial anomalies associated with this genetic condition present significant challenges for the oral health of patients. A detailed understanding of these changes is crucial for the development of appropriate therapeutic approaches and management strategies, as well as early intervention and specialized dental follow-up are key to improving the quality of life of these individuals, integrating dental care with a multidisciplinary approach that addresses the multiple needs of patients with this anomaly.

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