Research, Society and Development, v. 9, n. 9, e916998052, 2020
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v9i9.8052

Cleidocranial dysplasia- case report

Displasia cleidocraniana- relato de caso

Displasia cleidocraneal- reporte de caso

Received: 09/02/2020 | Reviewed: 09/07/2020 | Accept: 09/11/2020 | Published: 09/13/2020

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Abstract

Cleidocranial dysplasia (CCD) is a rare syndrome, occurring at a rate of 1:10,000,000 in the form presented in this clinical case. This syndrome occurs due to an autosomal dominant

inheritance characterized by changes in skeletal formation and development, as a result of a mutation associated with the RUNX2 gene, the main regulatory gene for osteoblastic differentiation, resulting in manifestations such as hypoplastic or aplastic clavicles, brachycephaly, hypoplasia of the middle third of the face, and delay or non-closure of fontanelles. Specifically, in the intraoral region, atypical dental manifestations occur, such as failure in the exfoliation of the primary dentition, delayed eruption of permanent teeth, and multiple supernumerary teeth. Thus, this study aims to present a case report of a patient with the pathognomonic characteristics of the syndrome in its rarest form, as well as the radiographic, imaging and clinical manifestations that allow its diagnosis and a discussion on the common manifestations in such patients, forms of treatment, and the conduct of treatment according to the specific needs of that case..

Keywords: Cleidocranial dysplasia; Teeth; Clavicle.

Resumo

A displasia cleidocraniana (CCD) é uma síndrome rara, ocorrendo a uma taxa de 1: 10.000.000 na forma apresentada neste caso clínico. Essa síndrome ocorre devido a uma herança autossômica dominante caracterizada por alterações na formação e desenvolvimento esquelético, em decorrência de uma mutação associada ao gene RUNX2, principal gene regulador da diferenciação osteoblástica, resultando em manifestações como clavículas hipoplásicas ou aplásticas, braquicefalia, hipoplasia do terço médio da face e retardo ou não fechamento das fontanelas. Especificamente, na região intraoral, ocorrem manifestações dentárias atípicas, como falha na esfoliação da dentição decídua, erupção tardia dos dentes permanentes e múltiplos dentes supranumerários. Assim, este estudo tem como objetivo apresentar o relato de caso de um paciente com as características patognomônicas da síndrome em sua forma mais rara, bem como as manifestações radiográficas, de imagem e clínicas que permitem o seu diagnóstico e uma discussão sobre as manifestações comuns nesses pacientes. formas de tratamento, e a condução do tratamento de acordo com as necessidades específicas daquele caso.

Palavras-chave: Displasia cleidocraniana; Dentes; Clavícula.

Resumen

A displasia cleidocraniana (CCD) é uma síndrome rara, ocorrendo a uma taxa de 1: 10.000.000 na forma apresentada neste caso clínico. Essa síndrome ocorre devido a uma herança autossômica dominante caracterizada por alterações na formação e desenvolvimento

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Palabras clave: Displasia Cleidocraniana; Dentes; Clavicula.

1. Introduction

Cleidocranial dysplasia (CCD) is an extremely rare syndrome occurring in every 1,000,000 births (Porciuncula et al., 2013). It is associated with mutations in the CBFA1 gene, currently known as RUNX2, present on chromosome 6p21. It is an autosomal and hereditary mutation, with random occurrences, without a family history, in 20-40% of cases. This gene controls the differentiation of precursor cells into osteoblasts, which explains the findings of the syndrome (Mundlos et al., 1995). The pathognomonic triad associated with this syndrome is composed of multiple supernumerary teeth, partial or total absence of clavicles, sagittal suture, and open fontanelles. The diagnosis of CCD is usually performed in a clinical setting, via imaging (El-gharbawy et al., 2011).

The syndrome is characterized by delayed closure of fontanelles and sutures, brachycephaly, frontal and parental prominence, hypoplasia of the maxilla and zygomatic arch, presence of Wormian bones, underdeveloped and narrow paranasal sinuses, ocular hypertelorism, and aplasia or clavicular hypoplasia. Bilateral clavicular agenesis is a rare manifestation, corresponding to 10% of cases, and allows hypermobility from the shoulders to the midline. Additionally, individuals affected by the syndrome may have short stature, pectus excavatum, valgus knees, scoliosis, defects in long bones, defects in the bones of the fingers, hypoplastic or absent nails, delay in the union of the mandibular symphysis, relative mandibular prognathism, arched, narrow and deep palate, and dental anomalies such as enamel hypoplasia, supernumerary teeth, ectopic dental location, non-eruption, and abnormal morphology, mainly radicular, of permanent teeth and prolonged retention of primary

dentition (El-gharbawy et al., 2011; Jaruga et al., 2016; Kreiborg et al., 2018; Lu et al., 2015; Mundlos et al., 1995; Mundlos, 1999). Nevertheless, clinical manifestations and intensity may vary between affected patients due to the variable expressiveness of the syndrome (El-gharbawy et al., 2011; Lu et al., 2015; Porciuncula et al., 2013).

This article consists of a case report, with photographic, radiological and tomographic documentation relating to a patient with CCD who presents all the pathognomonic characteristics of this syndrome and the complete absence of clavicles, which makes this case even rarer.

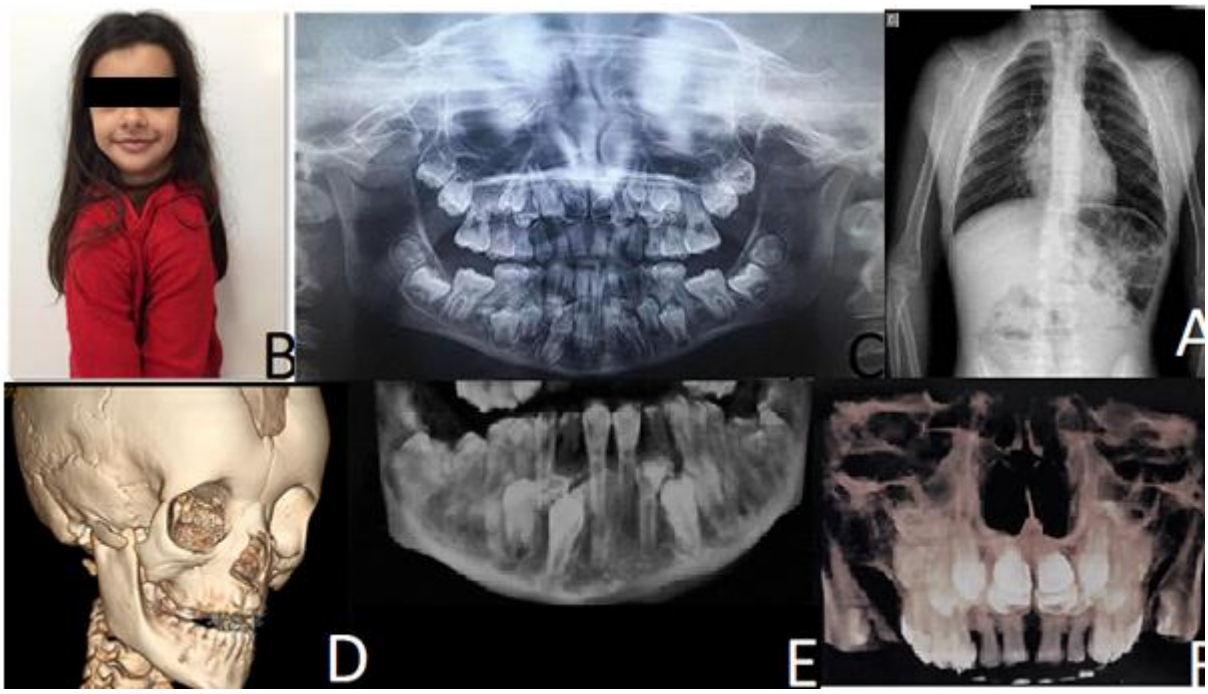
2. Methodology

This is a descriptive, detailed and retrospective image study, carried out using the direct observation technique. (Pereira et al., 2018), being one of the most basic and traditional forms of clinical study in the medical fields. Patient data were collected at the hospital with anamnesis and requested tests. Following ethical principles, the patient and his family consented to the dissemination of data and the display of images of their case for academic purposes by signing a Free and Informed Consent Form.

3. Case Report

The patient is female, 11 years of age, presenting melanoderma, and diagnosed with Cleidocranial Dysplasia (CCD). She was referred to the service for a multidisciplinary dental evaluation and preparation of an appropriate treatment plan. She did not have a family history, according to the legal guardian. Clinically, the patient had phenotypic characteristics of the syndrome, such as depression in the fontanelle region, maxillary atresia, asymmetry of the ala nasi, hypermobility of the shoulders, allowing them to be touched between at the midline, which characterizes bilateral absence of the clavicles, deformities of the toes, and thoracolumbar deformity with hyperconcavity. The findings were confirmed by imaging examinations of the face and chest (Figures 1A, B, C, D, E, F).

Figura 1. A-Radiografia Postero Anterior de Tórax evidenciando a ausência clavicular bilateral.1 B) Paciente com Síndrome de Displasia Cleidocraniana em vista frontal. Nota-se a hipermobilidade dos ombros caracterizando aplasia clavicular bilateral, atresia do terço médio, depressão na região de fontanela e hipertelorismo aparente. C) Exame radiográfico panorâmico com presença de dentes supranumerários, manutenção de dentição decídua e impactação da dentição permanente Figura 1D- Recontrução de tomografia de face evidenciando a região de fontanela aberta e formação do arco zigomatico apenas no segmento temporal. Figura 1E- Reconstrução tomográfica de tomografia cone beam em mandíbula Figura 1F- Recontrução de tomografia Cone bean em maxila.



Fonte: Autores.

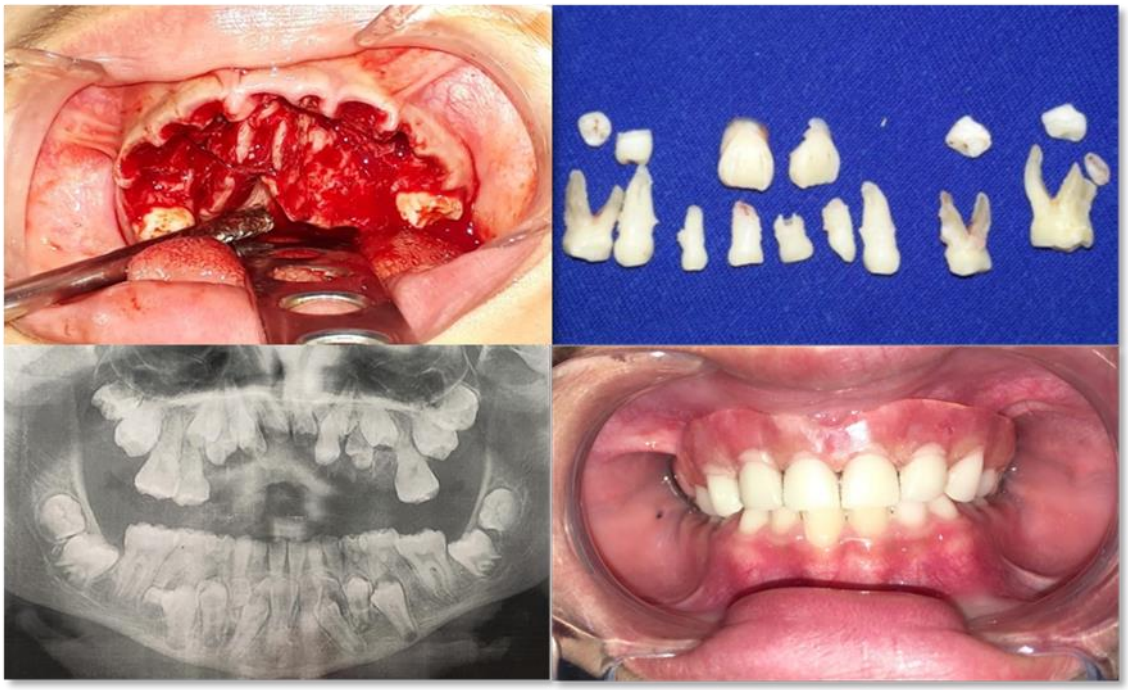
During the oral clinical examination, the presence of a mixed denture was found, with eruption of the first four permanent lower central molars and incisors and maintenance of the other upper and lower primary teeth (Figure 1C, E, F). The palate was narrow and deep, indicating maxillary underdevelopment. The patient's oral hygiene was satisfactory, with no need for interventions to adapt the oral environment.

When analyzing the imaging tests requested (panoramic radiography, PA radiography of the face and chest, computed tomography of the face, and cone-beam volumetric computed tomography), opening of the anterior fontanelle and coronal suture, scoliosis and hyperlordosis were observed, as well as prolonged retention of most permanent teeth, some with more than 2/3 of root formation and presence of several supernumerary dental elements – seven in the maxilla and six in the mandible, totaling thirteen. The location of supernumeraries was limited to the anterior region and premolars in both arches. As for the primary dentition, it was not in an advanced stage of root resorption, indicating that it would

not undergo exfoliation in the short term (Figure 1B, C, D, E, F).

The first phase of treatment consisted of extracting elements from the maxilla. All primary teeth were extracted, with the exception of the right second molar (Figure 2A). The permanence of this element contributes to the retention of the upper prosthesis, allowing the clamp to rest on it, as only the first permanent molar would not guarantee sufficient stability. Concomitant to simple extractions, the supernumeraries included were also extracted (Figure 2B and 2C). An acrylic prosthesis was made in order to return masticatory function, improve aesthetics and phonetics, and reinsert the patient into social life without major constraints, in addition to maintaining the vertical dimension and the space in the upper arch for the eruption of permanent teeth (Figure 2D).

Figura 2. A) Rebordo alveolar da maxila após extrações dentárias. B) Elementos decíduos e supranumerários extraídos. C) Radiografia panorâmica após a primeira intervenção cirúrgica. Observa-se a presença dos primeiros molares permanentes em cavidade oral, manutenção do dente 55 e demais elementos permanentes não erupcionados. D) Prótese provisória superior em acrílico instalada e adaptada.



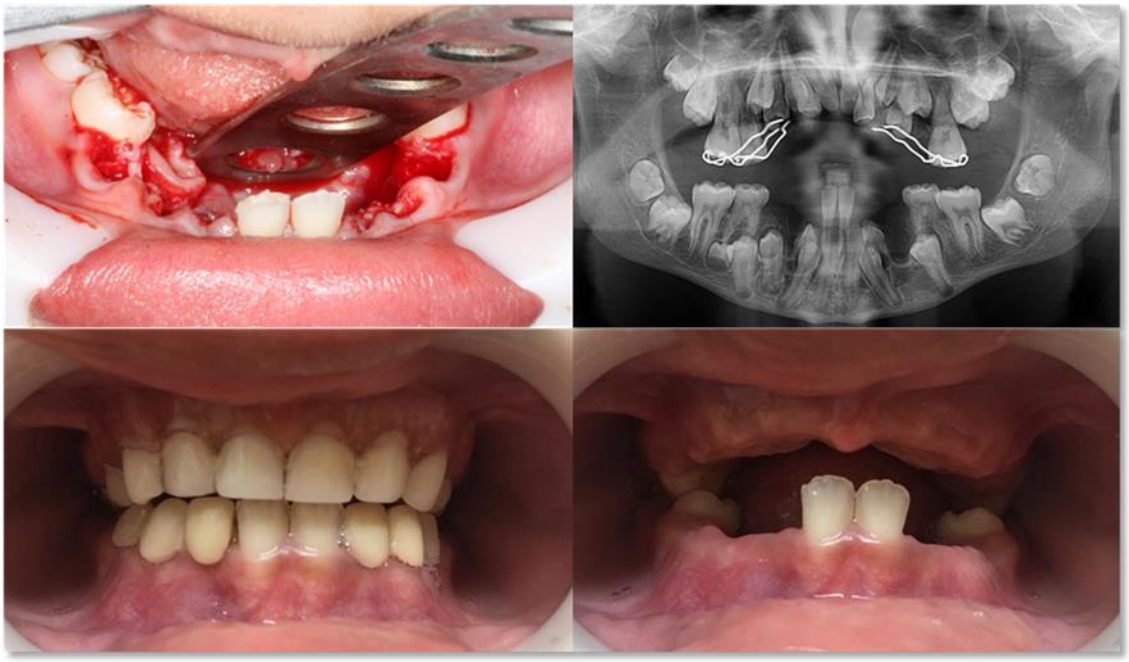
Fonte: Autores.

In the second surgical intervention, deciduous and supernumerary teeth included in the mandible were extracted, while the second deciduous molars and two supernumeraries were maintained due to their positions (Figure 3A and 3B). Moreover, after tissue recovery, an acrylic prosthesis was made with the same objectives as the upper one (Figure 3C). No bone

removal was performed to expose the retained permanent teeth, but rather solely to remove the supernumerary teeth.

Considering that permanent dentition has a potential for eruption due to its root formation, the case will be awaited and preserved through control of dental eruptions, prosthesis adaptations, and future orthodontic and surgical corrections to improve the ratio of bone and dental structures (Figure 3D).

Figura 3. A) Transcirúrgico das extrações em mandíbula. Observa-se a presença dos incisivos centrais inferiores permanentes, segundo molares decíduos e primeiros molares permanentes. B) Exame radiográfico panorâmico final. Nota-se a permanência de supranumerários (setados). C) Paciente com as próteses temporárias superior e inferior em oclusão. D) Rebordos alveolares após nove meses da primeira intervenção cirúrgica e três meses após as extrações em mandíbula.



Fonte: Autores.

4. Results and Discussion

The case report shows clinical and radiographic characteristics similar to the classic pictures of Cleidocranial Dysplasia, as described in the literature (El-gharbawy et al., 2011; Jaruga et al.,2016; Kreiborg et al., 2018; Lu et al., 2015; Porciuncula et al., 2013). The patient does not only present the pathognomonic triad, but also other phenotypic characteristics common to patients with the syndrome. A few skeletal changes were noticed at birth, while others were observed later, such as dental abnormalities related to the number of teeth and the

process of exfoliation and eruption of teeth. The early diagnosis of the syndrome allowed clinical and radiographic monitoring of the patient, favoring the design and execution of interventions at the most appropriate time (El-gharbawy et al., 2011; Lu et al., 2015).

The RUNX2 gene, present on chromosome 6p21, regulates not only the development of the skeleton, but also the expression of the mesenchymal tissue controlling the differentiation of the dental epithelium (Lu et al., 2015; Mundlos, 1999). Given its importance in the differentiation of osteoblasts, regression of the dental lamina following the development of the permanent teeth, osteoclastogenesis in the dental follicle region, and remodeling of the surface of the bones in the craniofacial complex, changes in this gene or in regulatory areas may partially explain the dental anomalies among patients with the syndrome (El-gharbawy et al., 2011; Mundlos, 1999; Roberts et al., 2013). The characteristic hyperdontia of the syndrome is the result of hyperactivity of the dental lamina, which causes excess epithelial buttons, a condition caused by a mutation in the RUNX2 gene, whose function is related to the proliferative activity of the lamina. Under normal conditions, the remains of epithelial cells undergo apoptosis during dental morphogenesis (El-gharbawy et al., 2011; Roberts et al., 2013).

Dental treatment of patients with Cleidocranial Dysplasia is interdisciplinary, prolonged, and unpredictable, requiring collaboration and maintenance of patient motivation (Berg et al., 2011; Park et al., 2013). The four main therapeutic approaches published in the literature are the Toronto-Melbourne, Belfast-Hamburg, Jerusalem and Bronx methods. The approaches differ in terms of the number of surgical interventions, timing of surgeries, grouping of teeth for orthodontic traction, and the use, or not, of temporary prostheses during treatment (Berg et al., 2011; Bufalino et al., 2012; Park et al., 2013). The treatment protocol used by the team is similar to the Bronx approach, consisting, in this phase, of two surgical moments, in which the primary dentition and the supernumeraries were removed under general anesthesia, followed by the manufacture of removable prostheses for aesthetic and functional purposes. As with other techniques, the phase of root development was considered for the start of the interventions (Roberts et al., 2013).

According to some reports, exposure and orthodontic traction are performed in the initial phase of treatment, concomitant with extractions or shortly thereafter, as it is considered that when bone resorption is reduced due to the RUNX2 mutation, the excessive distance between the eruption path and position are factors that negatively interfere with spontaneous eruption (El-gharbawy et al., 2011). It should be noted, however, that the potential for eruption of p atients' dental elements must be considered. Park et al. (2013)

described a case of a twelve-year-old patient, whose eruption had been awaited for more than nine months, but on whom orthodontic extrusion had to be performed due to the unfavorable position of some of the included elements.

5. Final Considerations

The case is still in progress, awaiting the spontaneous eruption of the permanent dentition. If this does not occur, new interventions will be carried out in order to expose surgically the elements for orthodontic traction, anchoring them in mini-implants and in previously erupted teeth.

Therefore, the treatment of patients with CCD often consists of a long-term approach involving several phases and health professionals, requiring a diagnosis in early childhood or prenatal phase in order to plan and perform all stages of treatment at the correct age. The individual should be able to present better development and maxillofacial prognosis, in addition to other changes and conditions pertaining to these patients.

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