Case Report: Cornelia de Lange Syndrome (CDLS)

Relato de Caso Síndrome Cornélia de Lange (CDLS)

Reporte de un caso de Síndrome de Lange (CDLS)

Marcelo Juliano **MORETTO**[1]
Tatyana de Souza **PEREIRA**[1]
Sandra Maria Herondina Coelho Ávila de **AGUIAR**[2]

[1] DDs, Ms Graduate Student, Department of Pediatric Dentistry, Araçatuba School of Dentistry, UNESP
[2]DDS, Ms, PhD Associate Professor, Department of Pediatric Dentistry, Araçatuba School of Dentistry, UNESP -

The Cornélia of Lange´s syndrome is a genetic anomaly, described and published by Cornelia Catharina of Lange in 1933, however, their aspects were described previously by Winfried Robert Clemens Brechmann in 1916, that's why it is also known as Brachmann of Lange's syndrome. The most frequent clinical characteristics include typical face dismorfia, variable degree of mental delay, anomalies of the hands and feet, multiple malformations, retardation of the pre and postnatal physical development and microcephaly variable intellectual compromising. Some facial characteristics are peculiar and they are mixed with the inherited lines of their own family, the united brows, the long lashes, the small nose, the round face, the fine lips and lightly inverted. As oral manifestations they present micrognathia, dental crowding, periodontal disease, delayed dental eruption, enamel hypoplasia, erosion of the enamel and dentine caused by stomach acids of the gastroesophageal reflux and atresia of the dental arches. The purpose of this paper is to present a clinical report of a boy bearer of this syndrome assisted at CAOE - FOA - UNESP, emphasizing the importance of multiprofessional team for the diagnosis and treatment of this syndrome.

Palavras chave: De Lange Syndrome; Oral Manifestations; Disabled Persons

INTRODUÇÃO

Cornelia de Lange syndrome (CDLS) or Brachmann - De Lange Syndrome (BDLS), first described in its full clinical presentation by Dr. Cornelia de Lange in 1933[1-5], is a multisystem syndrome involving congenital malformations, growth retardation and neurodevelopmental delay. Formerly, Brachmann[1-3] had observed a child at autopsy with similar features as well as additional findings of upper limb deficiencies. For the reason of their contributions, both Brachmann's and de Lange's names have been attached to the name of this syndrome[1-3,5]. It is a relatively uncommon syndrome.

Cornelia-De Lange Syndrome is a rare multiple congenital anomaly/mental retardation syndrome characterized by intrauterine fetal growth retardation, a variable phenotype and mutations in the gene NIPBL (NIPPED-B-like)[6-8].

The major criteria for CDLs are: the phenotype, including low frontal hairline and synophrys with high arched eyebrows, thin lips with protrusion of the upper lip, long and prominent philtrum, downturned corners of the mouth, small nose with anteverted nostrils, long eye lashes, low-set ears and micro and retrognathia; preand postnatal growth deficiency; internal anomalies of mainly the musculoskeletal system, ranging from tetraphocomelia or peromelia, bilateral monodactyly and ulnar agenesis to variable finger joint contractures and clubfeet and almost normal limbs; feeding dysfunction,

and psychomotor delay with a distinctive behavioral profile[8,9]. Structural and functional disorders of the inner organs include congenital heart defects, diaphragmatic defects, hearing impairment and gastro-esophageal reflux[8,10,11].

The incidence of CDLS is estimated at around 1 in 40,000 births[6-8] with a recurrence risk of less than one percent[2,8]. Despite this low recurrence, risk apprehension of the parents for subsequent pregnancies is usually high. Recurrences in siblings have been reported, but it is also sporadic.

The work of health professionals and parents is often hampered by lack of information about the disease, including its health complications. Most of these patients have lactose intolerance and difficulty eating, swallowing and digesting food. Many children have a reflux, which causes complications such as hiatus hernia or esophagitis[12].

Dental treatment is often overlooked in cases where the stomach acid causes dental problems such as erosion, making the teeth more susceptible to decay and gum disease[13]. Measures such as guidance and advice to parents tend to be most effective when applied at the time of birth of the child.

The objective of this study is to add to existing literature, plus a case of Cornelia de Lange syndrome, highlighting some aspects of the disease and the importance of multidisciplinary care.

CASE REPORT

In this particular instance, we did have a 12-year-old male patient with developmental disorder and speech impediment, who came with dental pain to the Center for Dental Care for People with Disabilities (Caoe) a Unit Assistant of the Araçatuba School of Dentistry, Paulista State University (UNESP). The male baby weighed about 1,750 g when he was born. He had also suffered malnutrition he had received the proper treatment during the first three months after delivery.

During the physical examination of the patient, we observed the main features of the syndrome recorded this data as follows:

• Pilosity on the forehead, eyebrows very thick, meeting in the midline and lashes very long and curved.
• Slightly anteverted nostrils.
• Lips thin and the presence of curvature less than the mouth at the expense of the angles facing down.
• Filtrum (nasolabial distance) increased.
• Ears small, dysplastic, rounded and slightly posterior position of deployment.
• Black hair abundant, low-set forehead and neck.
• Small and brachycephalic skull.
• Short neck.
• Pilosity marked throughout the body, most evident in the dorsal
• Short stature (Figures 1 and 2).

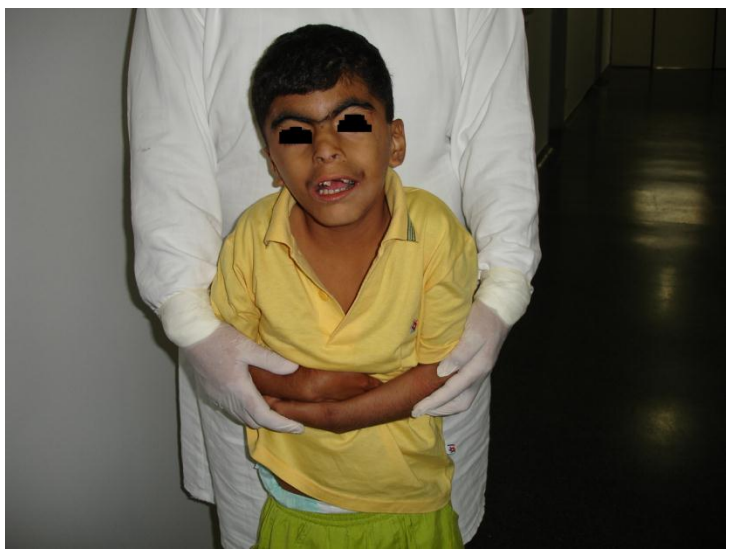

Figure 1 - Short stature

The behavior of the patient was evaluated by a psychologist, his personal interests, level of understanding, and pattern of relationships, tics and habits. From this analysis it was possible to trace the psychological profile of the patient.

A questionnaire was used to determine the conditions of birth and childhood of the individual, obtaining the following data:

• The mother was 25 and father 28 at the time of birth of the child,
• A child did not cry at birth,
• He was born premature from 7 to 8 months

• Born by caesarean
• There was need that the children remain in incubator for 18 days.
• Low weight 1750 kg at birth.
• No breastfeeding.
• Sucking and swallowing impaired.
• The child went only to 68 months.
• Never crawl
• He used a pacifier until 72 months
• Never had control of the sphincters.
• Restless sleep and insomnia
• Difficulties in understanding and hyperactivity
• No preference for sex or age
• Extremely hyperactive.
• Practice self-injury.
• The child responds to sounds
• Has visual difficulties
• Has difficulty swallowing chokes frequently during feeding.

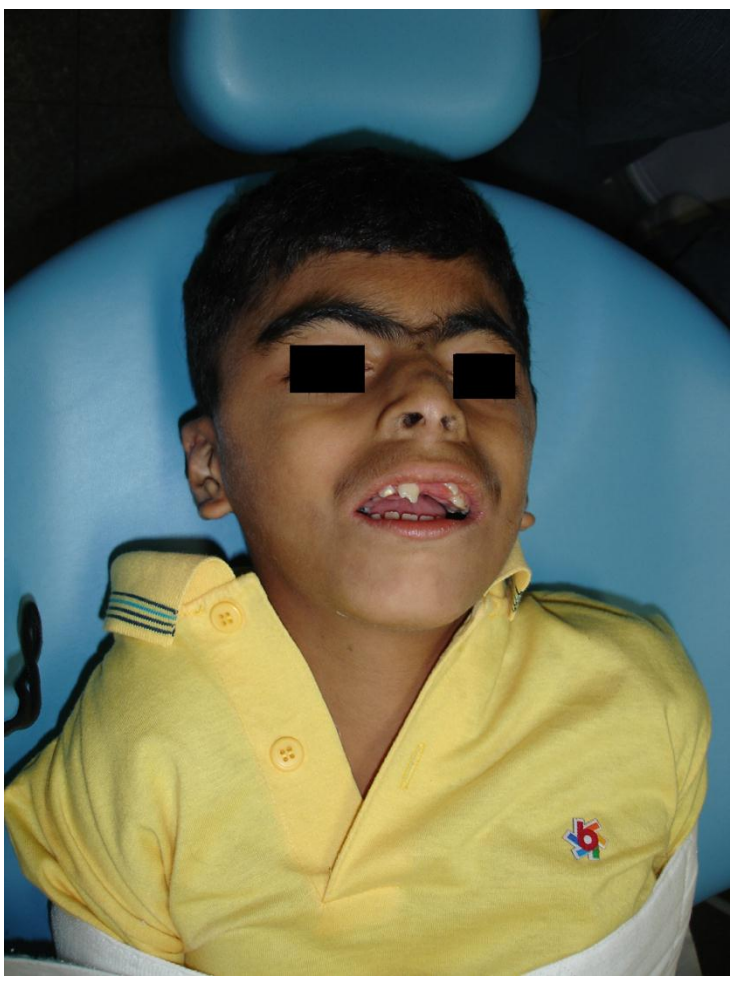

Figure 2 - Short stature

During the medical care performed by a general practitioner, cardiologist and neurologist were found slight systolic murmur, abnormal vision, and severe mental retardation during the interview and found that the mother had toxoplasmosis at the end of the 5th month of pregnancy.

The dental treatment was performed based on data obtained by the multidisciplinary team of CAOE, analyzing various factors such as degree of mental retardation, difficulty breathing and gastro esophageal reflux, determined that dental treatment could be done with physical restraint in an outpatient setting and against showing the procedures in the operating room with the use of sedation (Figures 3 and 4).

Figure 3 - Dental treatment with physical restraint and use of sedation

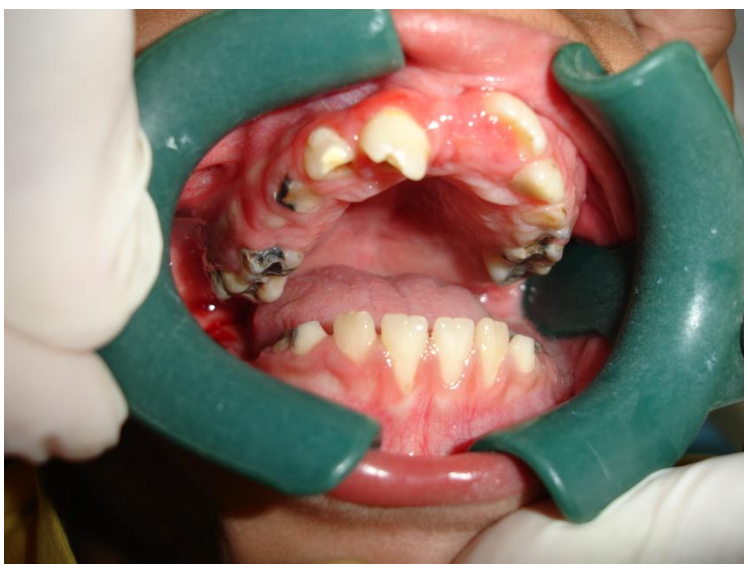

Figure 4 - Dental treatment

DISCUSSION

Accurate diagnosis of rare syndromes is a problem to be considered, because it is contradictory to the observed number of cases in countries considered developed and apparently non-existent in countries considered underdeveloped. A perfect diagnosis allows

appropriate treatment improving the life expectancy of individuals with syndromes and facilitating the work of professionals.

For our diagnosis process, the most essential diagnostic parameters seem to have been observed in respect of the face and limbs beyond the presence of severe mental retardation. The facial features concerning the long philtrum, thin lips and downturned angles of the mouth, micrognathia and anteverted nostrilsare usually noted even in mildly affected. The gastroesophageal reflux and sensorineural hearing loss are also common complications of the condition[4,15,16]. CDLS is generally accepted as being characterized by mental retardation associated with a characteristic group of physical malformations. Most cases described include severely deformed structures, although many of the physical manifestations may be present in members of a normal population[16].

Some dental abnormalities reported earlier include delayed eruption, spacing and macro- or microdontia.[16] Yamamoto et al.[16], have reported two cases with delayed tooth eruption and microdontia, with one of these cases being a partial anadontia. Also, there may be cardiovascular, endocrine and gastrointestinal abnormalities.

Van Allen et al.[9], proposed a classification system for CDLS in the classical (severe) or type I patients have intrauterine growth restriction, moderate psychomotor retardation and profound and severe malformations that can cause changes limiting and even death; (mild) or type II, CDLS patients have similar facial and minor skeletal abnormalities that were noted in type I; however, these changes may develop later or may be partially expressed in type III includes the patients who have phenotypic manifestations of CDLS, which are causally related to chromosomal aneuploidies or teratogenic exposures. Based on the given classification, our case falls into type II.

During this search, we have realized that there were a few citations on the dental and oral findings of the Cornelia de Lange syndrome. Since the literature regarding the CDLS was poor, it appears that the relationship between the oral manifestations of this syndrome and other syndromes must be further investigated.

CONCLUSION

In conclusion, all the findings in this study may lead us to believe if the multidisciplinary treatment is extremely important in cases of Cornelia de Lange Syndrome, as well as additional comfort to the patient provides valuable information that can and should be used by other professionals to better diagnosis and treatment of complications associated with this syndrome. A perfect diagnosis allows appropriate treatment improving the live expectancy of individuals with syndromes and facilitating the work of professionals.

RESUMO

A Síndrome da Cornélia de Lange é uma anomalia genética, descrita e publicada por Cornelia Catharina de Lange em 1933. No entanto, seus aspectos foram descritos anteriormente por Winfried Robert Clemens Brechmann em 1916, razão pela qual também é conhecida como Síndrome Brachmann de Lange. As características clínicas mais freqüentes incluem dismorfia facial típica, grau variável de atraso mental, anomalias das mãos e pés, malformações múltiplas, retardo do desenvolvimento pré e pós-natal físico e microcefalia variável com comprometimento intelectual. Algumas características faciais são peculiares e são misturadas com as linhas herdadas de sua própria família: sobrancelhas unidas, longos cílios, nariz pequeno, face redonda, lábios finos e levemente invertidos. Como manifestações bucais apresentam apinhamento dentário, micrognatia, doença periodontal, a erupção dentária retardada, atresia das arcadas dentárias, hipoplasia do esmalte e erosão do esmalte e dentina causados pelos ácidos provenientes do refluxo gastroesofágico. O objetivo deste trabalho é apresentar um caso clínico de um menino portador da síndrome atendido no CAOE - FOA - UNESP, enfatizando a importância da equipe multiprofissional para o diagnóstico e tratamento desta síndrome.

Palavras chave: Síndrome de Lange; Manifestações bucais; Pessoas com deficiência.

RESUMEN

El Síndrome de Cornelia de Lange es una anomalía genética, descrita y publicada por Catharina Cornelia de Lange en 1933. Sin embargo, los aspectos se han descrito previamente por Winfried Robert Clemens

Brechmann en 1916, por lo que también se conoce como síndrome de Brachmann Lange. Las características observadas con mayor frecuencia son la cara con dismorfia típica, grado variable de retraso mental, anomalías de las manos y los pies, las malformaciones múltiples, retraso en el desarrollo pre y postnatal y microcefalia físico con discapacidad intelectual variable. Algunas de las características faciales son únicos y se mezclan con las líneas heredadas de su familia: cejas unidas, pestañas largas, nariz pequeña, cara redonda, labios delgados y revirtió levemente. Las manifestaciones orales incluyen apiñamiento de dientes, micrognatia, la enfermedad periodontal, la erupción dental retardada, atresia de las arcadas dentarias, hipoplasia del esmalte y erosión del esmalte y la dentina causada por el ácido del reflujo gastroesofágico. El objetivo de este trabajo es presentar un caso clínico de un niño portador del síndrome visto en el Perro y - FOA - UNESP, haciendo hincapié en la importancia del equipo multidisciplinario para el diagnóstico y tratamiento de este síndrome.

Palabras clave: Síndrome de Lange; Manifestaciones Bucales; Personas con Discapacidad

REFERÊNCIAS

1. Braddock SR, Lachman RS, Stoppenhagen CC, Carey JC, Ireland M, Moeschler JB, et al. Radiological features in Brachmann-de Lange syndrome. Am J Med Genet 1993 15;47(7):1006-13.
2. Jackson L, Kline AD, Barr MA, Koch S. de Lange syndrome: a clinical review of 310 individuals. Am J Med Genet 1993 15; 47(7):940-6.
3. Huang WH, Porto M. Abnormal first-trimester fetal nuchal translucency and Cornelia De Lange syndrome. Obstet Gynecol 2002; 99(5 Pt 2):956-8.
4. Sakai Y, Watanabe T, Kaga K. Auditory brainstem responses and usefulness of hearing aids in hearing impaired children with Cornelia de Lange syndrome. Int J Pediatr Otorhinolaryngol 2002 21; 66(1):63-9.
5. Toker AS, Ay S, Yeler H, Sezgin I. Dental findings in Cornelia de Lange syndrome. Yonsei Med J 2009 30; 50(2):289-92.
6. Krantz ID, McCallum J, DeScipio C, Kaur M, Gillis LA, Yaeger D, et al. Cornelia de Lange syndrome is caused by mutations in NIPBL, the human homolog of Drosophila melanogaster Nipped-B. Nat Genet 2004;36(6):631-5. Epub 2004 May 16.
7. Tonkin ET, Wang TJ, Lisgo S, Bamshad MJ, Strachan T. NIPBL, encoding a homolog of fungal Scc2-type sister chromatid cohesion proteins and fly Nipped-B, is mutated in Cornelia de Lange syndrome. Nat Genet 2004; 36(6):636-41. Epub 2004 May 16.
8. Schiffer C, Schiesser M, Lehr J, Tariverdian G, Glaeser D, Gabriel H, Mikuz G,Sergi C. Unique occurrence of Brachmann-de Lange syndrome in a fetus whose mother presented with a diffuse large B-cell lymphoma. Pathol Oncol Res 2007; 13(3):255-9. Epub 2007 Oct 7.
9. Van Allen MI, Filippi G, Siegel-Bartelt J, Yong SL, McGillivray B, Zuker RM, Smith CR, Magee JF, Ritchie S, Toi A, et al. Clinical variability within Brachmann-de Lange syndrome: a proposed classification system. Am J Med Genet 1993; 47(7):947-58.
10. Ireland M, Donnai D, Burn J. Brachmann-de Lange syndrome. Delineation of the clinical phenotype. Am J Med Genet 1993 15; 47(7):959-64.
11. Nowaczyk MJ, Mohide P. Brachmann-de Lange Syndrome. McMaster University Prenatal Diagnosis Rounds. Front Fet Heath 2001; 3 (www.sickkids.on.ca)
12. Nakamura A.M, Síndrome de Cornélia de Lange. Rev AONP. 2001; 7.
13. Dossier: doenças raras em Portugal . Rev e-ciência , 2005; 44:22-5.
14. Zankl A, Rampa A, Schinzel A. Brachmann-de Lange syndrome (BDLS) withasymmetry and skin pigmentary anomalies: a result of mosaicism for a putative bdls gene mutation? Am J Med Genet A. 2003; 118A(4):358-61.
15. Barrett AW, Griffiths MJ, Scully C. The de Lange syndrome in association with a bleeding tendency: oral surgical implications. Int J Oral Maxillofac Surg 1993; 22(3):171-2.
16. Yamamoto K, Horiuchi K, Uemura K, Shohara E, Okada Y, Sugimura M, et al. Cornelia de Lange syndrome with cleft palate. Int J Oral Maxillofac Surg 1987; 16(4):484-91.

Correspondência

Profª.Drª. Sandra maria Herondina Coelho Ávila de Aguiar

Faculdade de Odontologia de Araçatuba,UNESP

saguiar@foa.unesp.br