Brachman de Lange syndrome

Leena Verma, Sidhi Passi, Krishan Gauba

Abstract

Brachman de Lange syndrome or Cornelia de Lange syndrome (CdLS) is a genetic disorder which can lead to severe developmental anomalies. It affects both the physical and intellectual development of a child. It is characterized by skeletal, craniofacial deformities, gastrointestinal and cardiac malformations. This syndrome is of rare occurrence and affects between 1/10,000 and 1/60,000 neonates. Diagnosis is based on the characteristic phenotype, in particular, a striking facial appearance, prenatal and postnatal growth retardation, various skeletal abnormalities, hypertrichosis, and developmental delay. Here, we present the case of a 13-year-old patient, with micrognathia, delayed eruption, multiple carious teeth, missing teeth and periodontal problems together, which had never been reported before. The father was also found to have the same missing teeth as the girl child.

Keywords: Cornelia de Lange, dental caries, partial anodontia

Introduction

The first ever documented case of Cornelia de Lange syndrome (CDLS) was in 1916 by W. Brachmann, followed by Cornelia de Lange, a Dutch pediatrician, in 1933, after whom the disorder has been named Cornelia de Lange syndrome. It is a rare multiple congenital anomaly affecting between 1/10,000 and 1/60,000 neonates.[1-3] It has characteristic abnormalities, including microcephaly, growth failure, anomalies of development of the hands and feet, short stature, excessive growth of hair, heavy eyebrows, micrognathia, downturned mouth, hirsutism.[2,4] The dental problems include ogival palate, little development of the mandible, dental malalignment, delayed tooth eruption, microdontic teeth, periodontal disease and dental erosion produced by frequent gastric reflux. The clinical diagnosis of this syndrome is based mainly on a group of these features; there are no biochemical or chromosomal markers for CDLS yet.

Here, we present a case report of a 13-year-old child diagnosed with CDLS.

Department of Pedodontics, Dr. H.S.J. Institute of Dental Sciences and Research, Chandigarh, India.

Correspondence: Dr. Sidhi Passi,
House No. 119, Sector 21-A, Chandigarh, India.
E-mail: sidhi.passi@gmail.com

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Case Report

A 13-year-old girl reported to Dr. H.S. Judge Institute of Dental Sciences, Panjab University, Chandigarh, with the chief complaint of carious teeth. History revealed that the child was the elder of the two siblings whose parents had no history of consanguinity, and was born at full term by normal delivery. Her parents and younger brother appeared normal. After birth, the child was noted to have poor general health, delayed milestones and used to fall sick frequently. The child was diagnosed with CDLS at 4 years of age. During the physical examination of the patient, we recorded the following data:

- Weight: 25 kg,
- Height: 125 cm,
- Head circumference: 47 cm and
- Pulse: 108 beats/minute.

Her face seemed dysmorphic and had thick curly hair, eyebrows meeting at the midline, along with long curved eyelashes [Figure 1]. Her ears were abnormally low placed, dysplastic, and mandibular symphysis was bumpy [Figure 1]. She also had anteverted nostrils, a small nose, thin lips with the downward turned angles of the mouth, micrognathia, short neck, fairly small feet and hands [Figure 2], and some hirsutism on her arms and legs. The patient scored 64 on the intelligence quotient (IQ) test, which fell into the interval of 44–75. She neither had the muscular capacity that a 13-year-old should have nor could communicate. The patient also had microcephaly and was only able to understand the basic words and some phrases. During evaluation, cardiovascular and respiratory systems did not show any abnormality. EEG report showed mental retardation. Behavioral findings showed that she loved to play alone and does not mix with other children. Orthopantomograph (OPG) and lateral cephalometric radiograph was advised [Figures 3 and 4]. The child had multiple retained deciduous teeth and showed missing permanent teeth on OPG. Oral examination showed the following:

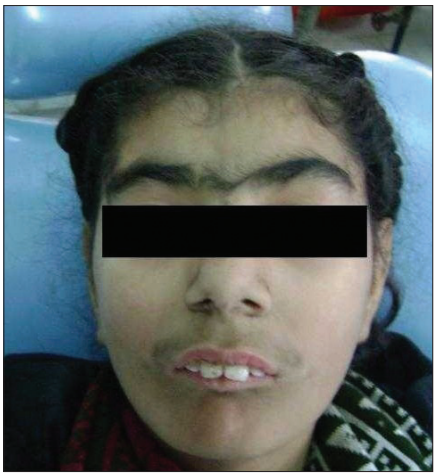

Figure 1: Facial appearance of patient with Cornelia de lange syndrome

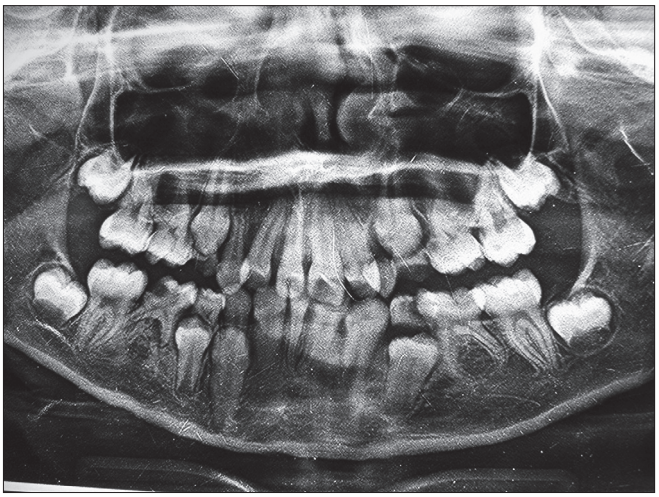

Figure 3: OPG showing multiple retained deciduous teeth and missing permanent teeth

Teeth present

16,55,54,53,12,11	21,22,63,64,65,26
46,85,84,83,42,41	31,32,33,74,75,36

Missing teeth

15	23, 25
45	35

Carious teeth

55	65
75, 74	85

Other features included prognathic maxilla, protruded maxillary anterior teeth, delayed dentition, deep palate, along with short vertical facial height [Figure 5]. OPG of the father also revealed same missing teeth as that of the girl child [Figure 6]. Cast models of both upper and lower

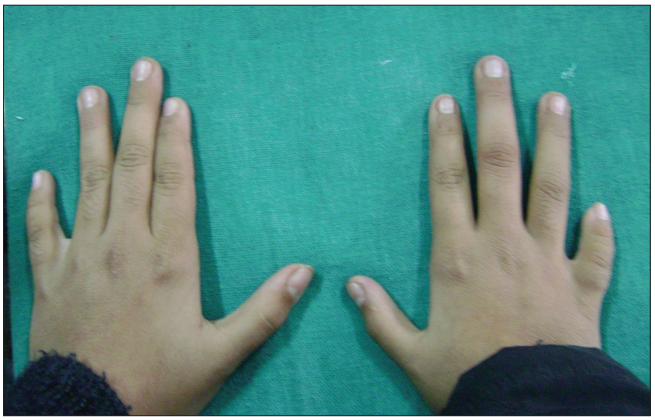

Figure 2: Clinodactyly of the fifth finger

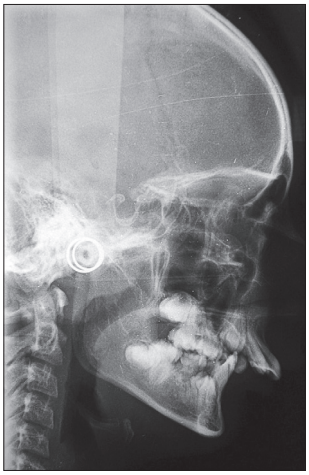

Figure 4: Lateral cephalometric radiograph showing prognathic maxilla and protruded maxillary teeth

dentition were made for case study and for further treatment planning. Behavior management of the child was a challenge as the child was very hyperactive, fidgety, had a low attention span, In the first dental visit, no treatment was initiated and only familiarization with the dental clinic environment was done. Subsequent appointments were especially scheduled in the mornings. Demonstration of brushing technique was given to the parent and importance of maintenance of good oral hygiene was explained and reinforced at subsequent visits. Restoration of the affected teeth along with sealant application was done. Treatment completed in multiple visits as the child could not sit for long.

Discussion

Cornelia de Lange is a rare congenital disorder with an incidence between 1/10,000 and 1/60,000 neonates. There are only a few reports on the dental and oral findings of the CDLS, suggesting its rare occurrence. The clinical features include mental retardation, skeletal defects (including brachycephaly, hypoplastic mandible and cleft palate), ocular defects, epilepsy

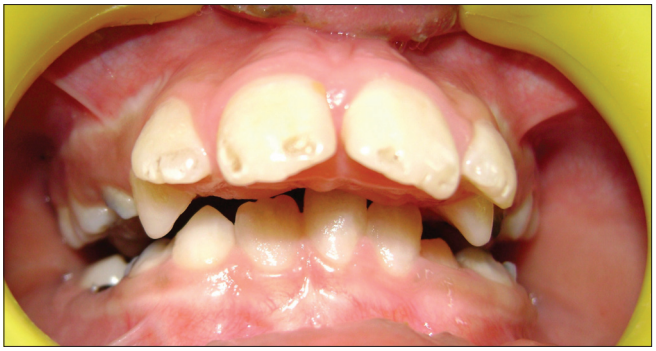

Figure 5: Intraoral appearance of the patient.

and varying degrees of hirsutism. The eyebrows may be joined across the bridge of the nose (synophrys), in addition to hypertelorism and antimongoloid slant of the eyes, upward facing nostrils, and thin lips, which help us diagnose CDLS. The gastroesophageal reflux and sensorineural hearing loss are also common complications of the condition.[4] The case we have described here presents the principal clinical characteristics of this syndrome. The diagnosis of CDLS is primarily a clinical one based on signs and symptoms.

Recently, genes responsible for CDLS have been discovered. They are as follows.

- *NIPBL* on chromosome 5 discovered in 2004;
- *SMC1A* on X chromosome discovered in 2006 and
- *SMC3* on chromosome 10 discovered in 2007.

The latter two genes seem to correlate with a milder form of the syndrome. The vast majority of cases are due to spontaneous mutations, although the defected gene can be inherited from either parent, making it autosomal dominant. Two phenotypes of CDLS have been recognized. They are
CDLS type I – classic and
CDLS type II – mild.

The prognosis for patients with the mild phenotype is much better than that for patients with the classic form.[5] Diagnosis and counseling for CDLS is complicated by the phenotypic variability and lack of a definitive diagnostic marker. The clinical phenotype has been shown to be quite variable. The full phenotypic spectrum will not be evaluated until the gene is identified and a possibility of molecular confirmation of the diagnosis appears.

Some dental abnormalities reported earlier include delayed eruption, spacing, missing teeth, micrognathia and macro or microdontia. Yamamoto *et al*.[1] have reported two cases with delayed tooth eruption and microdontia, with one of these cases being a partial anodontia. In our case, we have found micrognathia, delayed eruption and partial anodontia together. More distinctively, as compared to the previous cases, our case had the same missing permanent teeth as her father.

As a presentation of different types of CDLS, Van Allen *et al*.[6] proposed a classification system. Type I "classic" patients have the characteristic facial and skeletal changes of CDLS. Type II "mild" CDLS patients have similar facial and minor skeletal abnormalities as that of type I; however, these changes may develop later or may be partially expressed. Type III phenocopies CDLS 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.

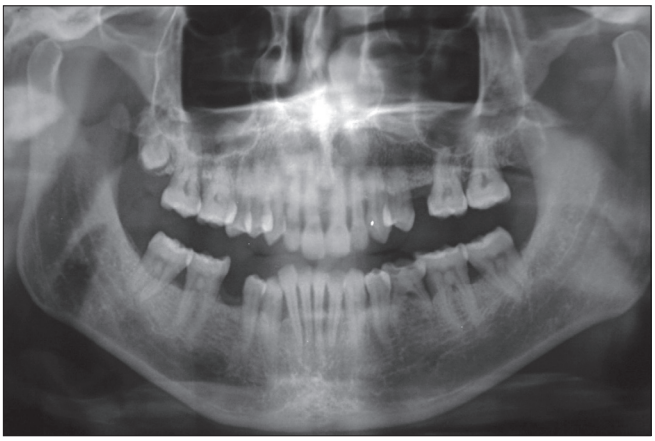

Figure 6: OPG of the father showing the same missing teeth as in the patient's OPG

In conclusion, preventative revisions starting in infancy and in coordination with the pediatrician are necessary. Routine revisions done every 6 months facilitate the changes in orofacial growth, detection of pathologies and strengthen the care of teeth at home.

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