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CASE REPORT

A Cornelia de Lange Syndrome Patient with Cleft Palate: A Case Report with Intraoral and Extraoral Findings

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Abstract

Objective: This case report presents the clinical and genetic findings in a one-week-old male patient with Cornelia de Lange Syndrome (CdLS) and unilateral cleft palate with a review of literature which includes case reports with cleft lip and palate.
Case Presentation: The patient exhibited characteristic facial dysmorphism, including a low-set hairline, long and bushy unibrow, inclined nose with anteverted nostrils, long philtrum, thin lips, and micrognathia. Upper limb malformations, genitourinary anomalies, and hirsutism were also present. The patient underwent comprehensive follow-up for five months, during which an alginate impression was taken to aid intraoral feeding, and a plaster model was prepared for the construction of an obturator, an essential component of the cleft palate management plan. The treatment plan involved multidisciplinary collaboration, including pre-surgical orthodontic preparation, evaluation of dental anomalies, surgical intervention with an oral and maxillofacial surgeon, post-operative care, and monitoring. Post-surgical orthodontic treatment and speech therapy were planned for later stages, followed by fine-tuning and a retention plan for long-term stability.
Conclusions: CdLS is a complex genetic disorder characterized by various physical abnormalities. This case report demonstrated the management of a one-week-old male patient with CdLS and unilateral cleft palate through a comprehensive multidisciplinary approach. Early intervention, personalized treatment plans, and long-term follow-up are crucial for addressing dental and maxillofacial complications associated with cleft palate in CdLS patients. Collaborative efforts among specialists yield optimal outcomes, improving the quality of life for individuals with CdLS and cleft palate.

Key words: cornelia de lange; cleft palate; cleft lip

Introduction

Cornelia de Lange Syndrome (CdLS), also known as Brachmann-de Lange syndrome, is a rare genetic disorder characterized by distinctive facial features, growth retardation, intellectual disability, and a wide range of physical abnormalities [1–20]. First described by Cornelia de Lange in 1933, CdLS has since become a subject of extensive research, allowing for a deeper understanding of its clinical presentation, etiology, and management [1–15,17–20]. CdLS is a genetically heterogeneous disorder primarily caused by mutations in genes involved in the cohesin complex, responsible for the proper chromosomal structure and gene regulation. These genetic alterations result in a wide spectrum of clinical phenotypes, making diagnosis challenging, particularly in milder cases or when atypical features are present [2,7,8,10,11,13,14,17,18].

The hallmark physical characteristics of CdLS include distinctive facial features such as synophrys (confluent eyebrows), long eyelashes, upturned nasal tip, thin upper lip, and microcephaly [3,5,6,19,20]. In addition to these craniofacial abnormalities, affected individuals may exhibit limb anomalies, including upper limb reductions, clinodactyly, or syndactyly [1,3,7,8,12,14,19,20]. Gastrointestinal complications, cardiac defects, hearing loss, and ophthalmologic abnormalities are also common in CdLS, underscoring the importance of a multidisciplinary approach to management [2,3,8,10–12,19,21]. The management of CdLS requires a collaborative effort involving various medical specialists, including pediatricians, geneticists, neurologists, orthopedic surgeons, speech and language therapists, and occupational therapists [4,10,19]. Early intervention, tailored educational programs, and comprehensive medical care can significantly improve the quality of life for individuals with CdLS and help mitigate the associated developmental delays and functional impairments [6,10,18].

This case report aims to present a comprehensive overview of a patient diagnosed with CdLS, focusing on the presence of cleft palate with clinical manifestations and the multidisciplinary approach employed in their care.

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Case Report

Ethical Approval: This case study exclusively employs a comprehensive examination of extant literature and publicly accessible resources pertaining to Cornelia de Lange Syndrome and its clinical presentations in infants. There was no direct engagement with the infant or any other human participants in this research, rendering ethical approval unnecessary. All endeavors have been undertaken to safeguard the privacy and confidentiality of data gleaned from the publicly available sources employed in this case study.

In this case report, clinical data collection and evaluation were carried out at Faculty of Dentistry, Department of Orthodontics. The case report was prepared according to the declaration of Helsinki and a written consent from the patient's family was taken.

A one-week-old male patient who was diagnosed with CdLS was referred to the Department of Orthodontics for the treatment of the unilateral cleft palate (Figure 1). Facial dysmorphism (low set hairline, long and bushy unibrow, nose with inclination, anteverted nostrils, long philtrum with thin lips, micrognathia) (Figure 2), upper limb malformations (short metacarpals, oligodactyly, micromelia), genitourinary anomalies, and hirsutism were present.

The patient has been undergoing a comprehensive follow-up at our clinic for a duration of five months. In order to facilitate the patient's intraoral feeding, an alginate impression was taken, and a plaster model was subsequently prepared (Figure 3). This model serves as a foundation for the construction of an obturator (Figure 4), which is an integral component of the treatment plan for cleft palate (CP) management.

As a result of genetic consultation, a putative pathogenic heterozygous variant has been identified in the NIPBL gene. The genetic diagnosis is consistent with autosomal dominant Cornelia de Lange syndrome type 1. According to the genetic test result, it is anticipated that the patient may experience various dental and maxillofacial complications. These complications are commonly associated with CP and may necessitate early dental interventions to address them effectively. Some of the reported complications include delayed persistent tooth eruption, malocclusion, microdontia, hypodontia, periodontal diseases, bruxism, and dental caries resulting from gastroesophageal reflux disease (GERD).

Delayed persistent tooth eruption is a frequently observed issue in individuals with CP. It refers to the delayed emergence of teeth beyond the normal expected time frame. This delay can be attributed to factors such as altered bone development, abnormal tooth positioning, or impaired tooth eruption mechanisms. Malocclusion, or improper alignment of the teeth and jaws, is another common complication associated with CP. It can result from a combination of factors including the cleft itself, abnormal growth patterns of the jaws, and discrepancies in tooth size and position. Malocclusion can lead to difficulties in chewing, speaking, and overall oral health. Microdontia and hypodontia are dental anomalies that can affect individuals with CP. Microdontia refers to abnormally small teeth, which can impact the overall aesthetics and function of the dentition. Hypodontia, on the other hand, involves the absence or incomplete development of one or more teeth. These conditions can contribute to further dental and occlusal irregularities.

In this article, we present a comprehensive orthodontic treatment plan for a patient with cleft palate and Cornelia de Lange syndrome. The treatment plan involves an initial consultation and diagnostic record collection, followed by treatment planning in collaboration with a multidisciplinary team. Pre-surgical orthodontic preparation and evaluation of dental anomalies is planned to be carried out in months three to four. The surgical phase will involve close collaboration with an oral and maxillofacial surgeon, with subsequent post-operative care and monitoring. Post-surgical orthodontic treatment, in conjunction with speech therapy, is planned in months seven to nine. The final stages of treatment focused on fine-tuning and detailing, leading to the formulation of a retention plan for long-term stability. The case highlights the

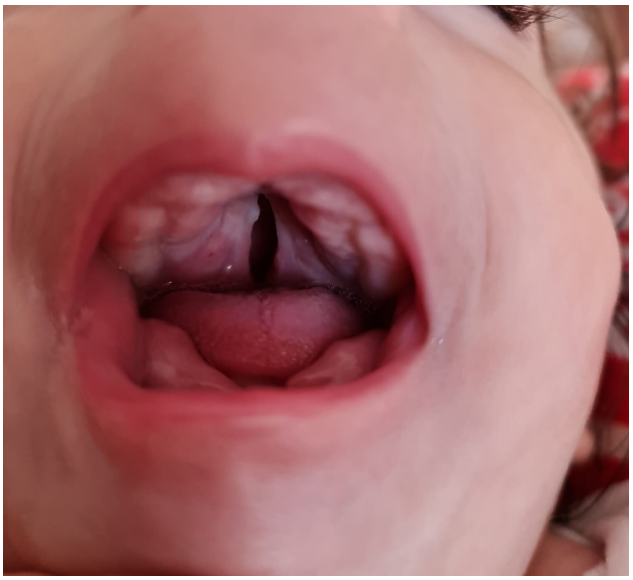

Figure 1. Intraoral image of the patient demonstrating a bifid uvula-type cleft palate.

Figure 2. Extraoral features of the patient (a-b).

essential role of orthodontics in managing complex craniofacial conditions, emphasizing the importance of interdisciplinary cooperation and long-term follow-up for optimal outcomes.

It is important to note that the treatment plan and timeline can vary based on the severity of the cleft palate, the individual needs of the patient, and the collaboration among the multidisciplinary team. The orthodontist's role throughout the process is to provide comprehensive orthodontic care, closely coordinate with other specialists, and ensure the best possible functional and aesthetic outcomes for the patient with cleft palate and Cornelia de Lange syndrome.

Discussion

A multidisciplinary approach involving dental professionals, orthodontists, maxillofacial surgeons, and other specialists is crucial to manage the dental and maxillofacial aspects of CP. Early inter-

Figure 3. Plaster model created from the alginate impression taken from the patient.

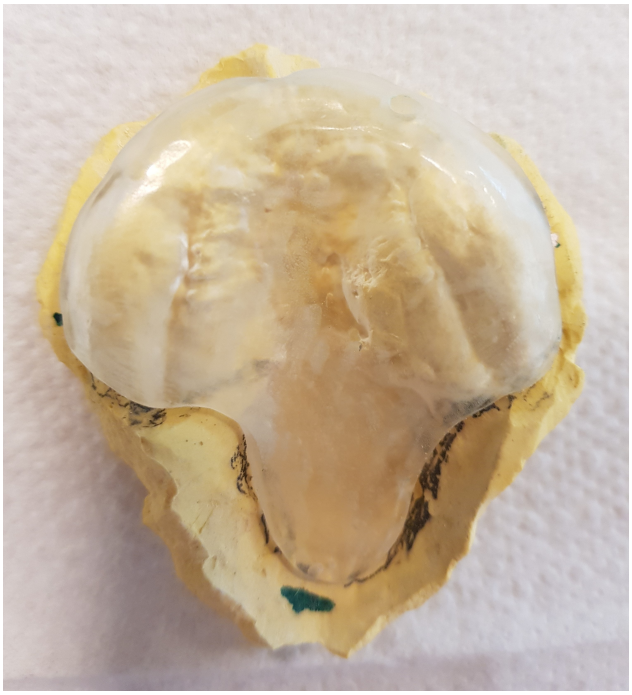

Figure 4. Acrylic obturator constructed for the patient.

vention, regular monitoring, and personalized treatment plans are essential to address these complications effectively, minimize oral health risks, and improve the overall quality of life for patients with CP.

Following a literature review on the PubMed database, several articles that reported CP in CdLS patients were evaluated. Table 1 presents various cases and aspects of CdLS, highlighting different features and associated findings observed in individuals with the syndrome. These features include CP, micrognathia inferior, face dysmorphism, upper extremity malformations, genitourinary anomaly, hirsutism, and other manifestations. Berg et al. reported that only 12% of the patients were born with cleft palate. Wenger et al. (2017) reported a case of CdLS in a 21-month-old female patient with left ventricular non-compaction cardiomyopathy, microform cleft lip, poor vision, and various other manifestations such as CP, micrognathia inferior, glossoptosis, face dysmorphism, upper extremity malformations, genitourinary anomaly, hirsutism, and oligodactyly[19]. Sataloff et al. (1990) reported the otolaryngologic manifestations of CdLS but did not specify individual patient data[16]. Park et al. (2010) reported a male CdLS patient with a mutation in the NIPBL gene. The patient was born at 32 weeks and presented with CP, micrognathia inferior, and other features such as upper extremity malformations, genitourinary anomaly, and hirsutism[14]. Yamamoto et al. (1987) reported multiple cases of CdLS with CP. The patients, all males, exhibited various CP types, submucous CP, bifid uvula, and other features such as glossoptosis, face dysmorphism, upper extremity malformations, genitourinary anomaly, and hirsutism[20]. Kline et al. (2007) reported a male patient who had an open cleft of the soft palate along with other features such as micrognathia inferior, face dysmorphism, upper extremity malformations, genitourinary anomaly, and hirsutism[10]. Kang et al. (2018) reported a female patient with CdLS and a severe phenotype. The patient had a complete cleft, along with other features such as micrognathia inferior and hirsutism[8]. Kim et al. (2005) reported a female patient with CdLS with CP, micrognathia inferior, genitourinary anomaly, hirsutism, and oligodactyly[9]. Galderisi et al. (2015) reported a case with micrognathia inferior, face dysmorphism, upper extremity malformations, genitourinary anomaly, and hirsutism. In their study, they focused on the resuscitation of a very low birth weight male infant with CdLS using the i-gel device[4]. Jezela-Stanek et al. (2019) reported a novel variant in the HDAC8 gene, resulting in a severe phenotype of CdLS in a male patient with micrognathia inferior, face dysmorphism, upper extremity malformations, genitourinary anomaly, and hirsutism[7]. Tranebjaerg et al. (1987) reported a case of CdLS in an 18-month-old female patient with a completely isolated CP along with other features such as micrognathia inferior, face dysmorphism, upper extremity malformations, genitourinary anomaly, and hirsutism[18]. Reilly & Carr (2001) reported a case with CdLS who ingested foreign body with severe developmental disabilities, including CP, micrognathia inferior, glossoptosis, face dysmorphisms, upper extremity malformations, genitourinary anomaly, hirsutism, oligodactyly[21].

Table 1. Literature review of patients with Cornelia De Lange syndrome and cleft palate.

Author	Date	Age	Gender	Presence of Cleft Palate	Cleft Palate Type	Micrognathia Inferior	Glossoptosis	Face Dysmorphism	Upper Extremity Malformations	Genitourinary Anomaly	Hirsutism	Oligodactyly
Tranebjærg et al.	1987	18 months	Female	Y	Complete Isolated Cleft Palate	Y	N	Y	Y	Y	Y	Y
		NA	Male	Y	Submucous Cleft Palate	N	N	Y	Y	Y	Y	Y
Yamamato et al.	1988	NA	Male	Y	Cleft of Hard and Soft Palate	N	N	Y	Y	N	Y	Y
		NA	Male	Y	Submucous Cleft Palate, Bifid Uvula	N	N	Y	Y	N	Y	Y
		NA	Female	Y	Bifid Uvula	N	N	Y	Y	Y	Y	Y
Reilly & Carr	2001	37 weeks	Male	Y	NA	Y	N	Y	Y	Y	Y	Y
Kim et al.	2005	18 years	Female	Y	NA	Y	N	Y	Y	Y	Y	NA
Kline et al.	2007	28 years	Male	Y	Open Cleft of the Soft Palate	N	N	Y	Y	Y	Y	Y
Park et al.	2010	32 weeks	Male	Y	NA	Y	N	Y	Y	N	Y	N
Galderisi et al.	2015	36 weeks	Male	Y	NA	Y	N	Y	Y	Y	Y	Y
Wenger et al.	2017	21 months	Female	Y	NA	N	N	N	N	N	Y	N
Kang et al.	2018	34 weeks	Female	Y	Total	N	N	N	Y	Y	Y	N
Jezela-Stanek et al.	2019	NA	Male	Y	NA	Y	N	Y	Y	Y	Y	Y

Conclusion

In conclusion, CdLS is a complex genetic disorder characterized by a wide range of physical abnormalities. This case report highlighted the management of a patient with CdLS and a unilateral CP through a multidisciplinary approach. Early intervention, personalized treatment plans, and long-term follow-up are crucial for addressing dental and maxillofacial complications associated with CP in CdLS patients. Collaboration among specialists is essential for optimal outcomes. Overall, comprehensive care can greatly enhance the quality of life for individuals with CdLS and CP.

Author Contributions

İ.E.: draft of the paper, data selection, patient follow-up, literature review G.Ü.: draft of the paper, data selection, literature review B.K.: supervision, critical review and editing

Conflict of Interest

The authors declare that there is no potential conflict of interest.

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