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Cornelia De Lange Syndrome – Case Report

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Abstract:
Cornelia de Lange syndrome (CdLS) is a complex genetic disorder characterized by distinctive facial features, delayed growth, and limb abnormalities. In 1916, Dr. W. Brachmann described the first case of this syndrome but in 1933 Cornelia de Lange, a Dutch pediatrician from Amsterdam was the first to report about two cases of this syndrome. It is also called Brachmann de Lange syndrome, Amsterdam dwarfism, Bushy syndrome. Craniofacial features commonly associated with CdLS include synophrys (joined eyebrows), arched eyebrows, long eyelashes, and microcephaly. The exact incidence is uncertain, but it is estimated to be 1 in 10,000 individuals, with no racial predilection. While most cases occur sporadically, familial transmission with an autosomal dominant inheritance pattern has been documented. A case of an 8-year-old girl with CdLS, exhibiting the typical facial and physical features of the syndrome, is reported herewith.

Keywords: *Cornelia de Lange syndrome, delayed growth, autosomal dominant inheritance, synophrys*

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I. Introducton

Cornelia de Lange syndrome (CdLS) is a rare genetic disorder that affects physical, cognitive, and behavioral triats. In 1916, Dr. W. Brachmann described the first case of this syndrome but in 1933 Cornelia de Lange, a Dutch pediatrician from Amsterdam was the first to report about two cases of this syndrome. It is also called Brachmann de Lange syndrome, Amsterdam dwarfism, Bushy syndrome [1]. The incidence is about 1 in 10,000 individuals, with no specific racial prevalence. CdLS is typically caused by mutations in one of seven genes: NIPBL, SMC1A, HDAC8, RAD21, SMC3, BRD4, and ANKRD11, which are involved in the cohesin complex's structure and function. Mutations in the NIPBL gene are found in 60% to 80% of cases [2].

The syndrome is primarily identified by distinct facial characteristics, such as a low anterior hairline, arched eyebrows, synophrys (joined eyebrows), anteverted nares, maxillary prognathism, a long philtrum, thin lips, a "carp" mouth, hirsutism, a high-arched palate, delayed eruption, crowding, missing teeth, dental caries, bruxism, spurs in the anterior angle of mandible and prominent symphysis in association with prenatal and postnatal growth retardation, psychomotor retardation/intellectual disability, and, in many cases, upper limb anomalies[3].

In this paper, we present the rare case of an 8-year-old female child diagnosed with Cornelia de Lange syndrome. This case report offers a brief overview of CdLS, highlighting its characteristic facial features and physical findings.

II. Case Report

An 8-year-old female child reported to the Department of Oral Medicine and Radiology of our Hospital, with the chief complaint of decayed teeth in both upper and lower jaws. Her medical history revealed that the child had low birth weight (2.2kg), dysmorphic facial features, laryngomalacia, severe anemia, supravalvular aortic stenosis, delayed developmental milestones as well as autistic and self-injurious behaviors. On eliciting her family history, it revealed that she was the only child born of non-consanguineous parents delivered by elective cesarean section.

On extraoral examination the child exhibited microcephaly, low anterior hairline, arched eyebrows, synophrys, a depressed flat nasal bridge, anteverted nares (Figure 1.a), low-set ears (Figure 1.b), a "fish-like" mouth with a long philtrum, thin lips, hirsutism, (Figure 1.c) and normal fingers with shortened third and fourth toes on both feet (Figure 2). The intraoral examination revealed a high arched palate, widely spaced teeth and dental caries affecting teeth 51,52,53,54,55,61,62,63,64,65,71,74,75,81,84,85 with erupting teeth 16,26,36,46. (Figure 3). The patient was uncooperative for dental panoramic radiograph.

III. Discussion

Cornelia de Lange syndrome (CdLS) is a rare genetic disorder that affects physical, cognitive, and behavioral traits. The syndrome was first described by Dr. W. Brachmann in 1916, but in 1933 Cornelia de Lange, a Dutch pediatrician from Amsterdam, who reported two cases of the disorder. The condition is also known as Brachmann de Lange syndrome, Amsterdam dwarfism, or Bushy syndrome [1]. The incidence of CdLS is about 1 in 10,000 individuals, with no specific racial predisposition. CdLS is typically caused by mutations in one of seven genes—NIPBL, SMC1A, HDAC8, RAD21, SMC3, BRD4, and ANKRD11—all of which are involved in the cohesin complex's structure and function. Mutations in the NIPBL gene are present in 60% to 80% of cases [2].

CdLS is primarily recognized by distinctive facial features, including a low anterior hairline, arched eyebrows, synophrys (joined eyebrows), anteverted nostrils, maxillary prognathism, a long philtrum, thin lips, a "carp" mouth, hirsutism, a high-arched palate, delayed eruption, spaced teeth, missing teeth, dental caries, bruxism spurs in the anterior angle of the mandible, and a prominent symphysis. These features are often associated with prenatal and postnatal growth retardation, psychomotor delays or intellectual disability, and, in many cases, upper limb anomalies [3]. Microcephaly, low anterior hairline, arched eyebrows, synophrys, a depressed flat nasal bridge, anteverted nares, a "fish-like" mouth with a long philtrum, thin lips, hirsutism, low-set ears and shortened third and fourth toes on both feet, delayed developmental milestones, dental caries, spaced teeth were found in our patient.

The syndrome can affect multiple systems, including the cardiac, gastrointestinal, craniofacial, genitourinary, musculoskeletal, and central nervous systems.[4]. Gastrointestinal issues commonly include gastroesophageal reflux disease (GERD), vomiting, belching, heartburn, and intermittent poor appetite. Vision problems may involve nystagmus, strabismus, ptosis, or myopia. Hearing impairments can range from mild to severe, often due to narrow ear canals that lead to chronic ear drainage. Cardiac defects, particularly congenital heart disease, are common, with ventricular septal defect being the most frequent. Mental challenges are also prevalent, with an average IQ of 53, placing individuals in the mild to moderate range of intellectual disability. Communication abilities are often affected, characterized by articulation errors, including sound substitutions and distorted or missing consonants. Other less common symptoms include seizures, hyperactivity, irritability, sleep disturbances, and self-injurious behaviors. The presence of severe developmental abnormalities is often a key factor in diagnosing the condition [5,6]. About 25–30% of children with CdLS are born with congenital heart defects. Additionally, individuals with CdLS may experience peripheral neuropathy, leading to a heightened pain threshold. Structural abnormalities of the kidneys or urinary tract, such as vesicoureteral reflux, pelvic dilatation, and renal dysplasia, are present in up to 40% of people with CdLS. Cardiovascular defects such as supravalvular aortic stenosis, delayed developmental milestones as well as autistic and self-injurious behaviors and poor appetite were found in our patient.

The initial diagnosis can be made through ultrasound between 20 and 25 weeks of gestation, with the most prominent abnormality being the absence or unusually short upper limb. A 3D ultrasound may also be performed, revealing characteristics such as long eyelashes, hypertrichosis (excessive hair growth), low-set ears, and micrognathia (a small jaw), which can interfere with the infant's ability to feed.[7] The diagnostic criteria for CdLS were established by the CdLS Foundation.[8]. The patient was diagnosed with Cornelia de Lange syndrome at one year of age based on its characteristic clinical features like arched eyebrows, synophrys, low-set ears, microcephaly, anteverted nares, a "fish-like" mouth with a long philtrum, thin lips.

The differential diagnosis for CdLS includes autism spectrum disorder, Rett syndrome, Roberts syndrome, Nicolaides-Baraister syndrome, DiGeorge syndrome, Fryns syndrome, CHOPS syndrome, Bohring-Opitz syndrome and fetal alcohol syndrome.[9]

Individuals with Cornelia de Lange syndrome (CdLS) face considerable challenges mainly due to the complex medical nature of the syndrome. They often require intensive management for a range of health issues, including gastrointestinal problems, cardiac anomalies, and developmental delays, all of which demand specialized care. Behavioral difficulties, such as self-injury and aggression, necessitate continuous monitoring and tailored behavioral management strategies.[10]

IV. Conclusion

The occurrence of CdLS places serious limitations on the lives of affected individuals. Life expectancy is relatively unaffected but if the patients develop any complications of the syndrome, then prognosis largely depends on the severity and management of that complication. Children often experience psychological lag and developmental delays, making a multidisciplinary approach essential for their care. An oral medical physician or a pediatric dentist may be the first healthcare professional to recognize a child with such issues and could take the lead in coordinating the multidisciplinary team to address their needs.

Images

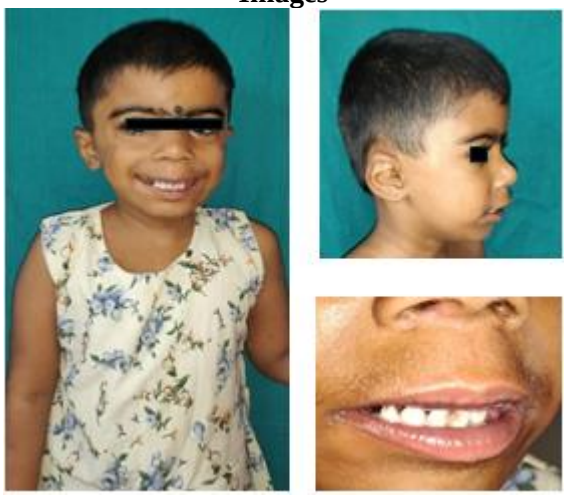

Figure 1. Extraoral Images Of Patient Showing (A) Microcephaly, Low Anterior Hairline, Arched Eyebrows, Synophrys, A Depressed Flat Nasal Bridge, Anteverted Nares, (B) Low-Set Ears, (C) "Fish-Like" Mouth With A Long Philtrum, Thin Lips, Hirsutism.

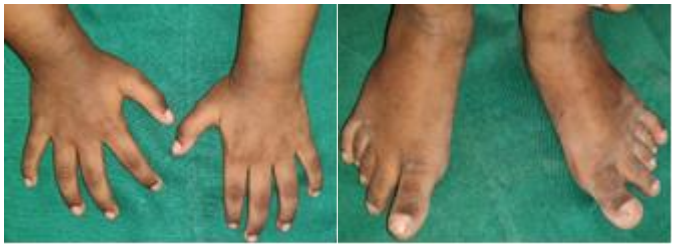

Figure 2 (A) Normal Fingers (B) Shortened Third And Fourth Toes On Both Feet

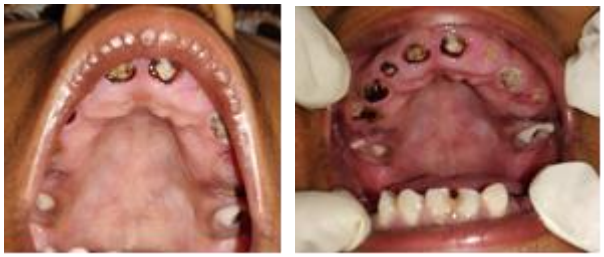

Figure 3: Intraoral Images Showing (A) High Arched Palate, (B)Dental Caries Affecting Both Upper And Lower Arches And Spaced Teeth

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