Cornelia de Lange Syndrome

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Abstract

Cornelia de Lange Syndrome (CdLS) affects many children today. It also fails to be diagnosed often until children are older. Ultrasound can be used to diagnose this prior to birth. There are many complications associated with CdLS including gastrointestinal problems as well as skeletal system anomalies. Once diagnosed, the child and family can prepare and take appropriate measures including speech, occupational, and physical therapy to take care of the child and his/her health.
Cornelia de Lange Syndrome

Cornelia de Lange Syndrome (CdLS) is a genetic anomaly that is present from birth. It is suggested that it occurs one in every ten thousand live births (Cornelia de Lange Syndrome Foundation, 2010c). It causes many physical malformations as well as mental, gastrointestinal, and behavioral complications. Cornelia de Lange syndrome was first described by Dr. Cornelia de Lange in 1933. CdLS is described as being, “a multisystem syndrome involving congenital malformations, growth retardation and neurodevelopmental delay” (Toker, Ay, Yeler, & Sezgin, 2009, p. 289).

How it Affects Children and Parents

If a child is born with CdLS and lives, there are things that can make living with the syndrome hard on the child as well as the parents. If a child has not been diagnosed with CdLS, their growth rate will be slower than their peers. Often it is just misdiagnosed as failure to thrive (Cornelia de Lange Syndrome Foundation, 2010b). Charts have been made available to doctors so they will be able to follow growth as compared to other affected individuals. Often with CdLS, parents/doctors notice there is a difference between them and their peers regarding appearance and behavior. This difference could lead to insecurity and isolation in that “Individuals with CdLS may exhibit increased levels of behaviors commonly associated with autism” (Richman, Belmont, Kim, Slavin, & Hayner, 2009, p. 550). When children with CdLS go through puberty, much of their behavior is the same as any teenager. However, they do exhibit worse behavioral problems and more aggression than normal (Cornelia de Lange Syndrome Foundation, 2010b).

As a parent, raising a child is a difficult task let alone having to raise a child with the complications of CdLS. Richman et al., (2009) performed a comparative analysis with stress of
parents of CdLS children and a control group of children without CdLS. They found, “It was clear that parents of children with CdLS experienced significantly higher levels of stress” (p. 551). However, though it may not be butterflies and roses, study suggests that there is an intervention and prevention strategy that can be used to deal with early childhood challenging behavior (Richman et al., 2009).

**Symptoms**

The symptoms of Cornelia de Lange Syndrome are very vast. This syndrome affects the entire body. Starting with the body systems, CdLS affects the cardiac, skeletal, gastrointestinal, vision and auditory systems. Studies show that the incidence of congenital heart disease in children with CdLS is as high as 20-30% percent when compared to the 0.08% for all births (Cornelia de Lange Syndrome Foundation, 2010b). Sometimes short stature and failure to thrive may be solely attributed to the syndrome, when congenital heart disease may be playing a part as well. The Cornelia de Lange Syndrome Foundation Web site recommends that every child with CdLS be seen and evaluated by a cardiologist (Cornelia de Lange Syndrome Foundation, 2010b).

The skeletal system is greatly affected by CdLS (See Fig. 1). It tends to either cause growth failure, or anomalies of development of the upper extremities. Clinodactyly on the toes and fingers is common (Toker et al., 2009). Small hands and limitations with regard to elbow motion are also seen. Some
children experience hip abnormalities that can affect/interfere with the ability to walk (Cornelia de Lange Syndrome Foundation, 2010b).

Patients also suffer from gastrointestinal problems. They often exhibit symptoms of vomiting, belching, heartburn, or intermittent poor appetite (Cornelia de Lange Syndrome Foundation, 2010b). Gastroesophageal Reflux Disease (GERD) is commonly diagnosed in those with CdLS. This can affect their appetite, social activities, and sleep.

Vision problems are usually easy to identify. Nystagmus, strabismus, ptosis, or myopia are a few of the vision impairments that can occur in CdLS. Nystagmus is shaky eyes. Strabismus is a misalignment of the eyes, most commonly turning in, or wandering out. Ptosis is where one or both eyelids droop, and sometimes surgery is recommended to correct this. Severe myopia or nearsightedness can occur but can easily be fixed with glasses. Children with any of these vision characteristics may become visually overwhelmed easily. Presenting things slowly can help with this (Cornelia de Lange Syndrome Foundation, 2010b).

Most children diagnosed with CdLS have mild to moderate or even severe hearing loss. These children have narrow ear canals which lead to problems with chronic ear drainage or cholesteatoma, a collection of skin cells in the ear. The use of CT scans can be used to see the severity of ear malformations. A computed tomography scan can see external auditory canal stenosis, soft
tissue opacification of the hypoplastic tympanomastoid cavity, dysmorphic ossicle, hypoplastic cochlea, and dysplastic vestibule (Kim, Kim, Lee, Lee, & Kim, 2008).

In addition to body system issues, there are also physical malformations. Hirsutism, or excessive hairiness, along with heavy eyebrows and long eyelashes is found with those diagnosed (See Fig. 2). Thin upper lip, cleft palate, deciduous teeth, and small nose are also associated with CdLS (Toker et al., 2009) (See Fig. 3). Mental issues are not uncommon. An average IQ score in individuals with CdLS is 53, which is within the mild to moderate range of mental retardation (Cornelia de Lange Syndrome Foundation, 2010b). The ability to communicate is hindered in those with CdLS. They exhibit errors in articulation, with sound substitutions and distorted or missing consonants. Though, speech is hard sometimes, access to early intervention programs and speech therapy can help (Cornelia de Lange Syndrome Foundation, 2010b).

**Diagnosing**

Diagnosing CdLS generally occurs after birth, with a clinical examination. But it can be very apparent and visualized through ultrasound. Initial diagnosis of the syndrome is usually made between 20 and 25 weeks of gestation (Kanellopoulos, Iavazzo, Tzanatou, Papadakis, & Tassis, 2011). When getting the ultrasound careful attention should be made to the face, hands, heart, arms, and ventricles of the head (Cornelia de Lange Syndrome Foundation, 2010b).
Syndrome Foundation, 2010a). The most obvious abnormality visualized is the upper limb because fingers and/or other bones might be missing or abnormally short (Cornelia de Lange Syndrome Foundation, 2010a). Often times, a 3-D examination with ultrasound are performed in conjunction with the routine ultrasound. 3-D examinations can reveal long eyelashes, low anterior and posterior hair line, micrognathia, where the jaw is small enough to interfere with the infants feeding, hypertrichosis, low set ears, irreducible flexion of the elbows, oligodactyly, and clinodactyly (Kanellopoulos et al. 2011). (See Fig. 4, 5, and 6). Other findings include problems in the heart such as atrial and ventricular defects and sometimes a diaphragmatic hernia or abdominal calcification (Cornelia de Lange Syndrome Foundation, 2010a).

**Treatments**

Once diagnosed, there are some treatments that should happen when diagnosed as well as throughout the individual’s life. At the time that the doctor/parent thinks the child might have CdLS, blood tests should be evaluated to be sure of the clinical diagnosis. One the diagnosis has been made, a few studies are recommended. Of these studies, the majority of them are performed in medical imaging: echocardiogram for the heart, renal ultrasound for the kidneys, and an upper GI series to rule out malrotation and reflux. Other tests not in medical imaging include hearing evaluation and a developmental assessment (Cornelia de Lange Syndrome Foundation, 2010b).
Additionally, in early childhood these patients should be regularly evaluated with their primary care provider. The Cornelia de Lange Foundation also recommends ongoing developmental services such as physical, occupational, and speech therapy. In addition, the foundation also highly suggest audiology testing every two to three years, repeat evaluation of GERD, a dental visit by a dentist familiar with patient needs, and an annual ophthalmology evaluation (Cornelia de Lange Syndrome Foundation, 2010b).

Once the individual is into late childhood, main treatment protocols are regular check-ups and upkeep. Orthopedic involvement may be necessary for joint contractures, hip complications, development of scoliosis, or orthotic use (Cornelia de Lange Syndrome Foundation, 2010b). When those with CdLS reach adulthood, they should have the same testing that those who do not have CdLS have. These include: blood pressure, electrocardiogram, breast, or testicular and prostate exams, and dental evaluations. One exam that CdLS diagnoses might consider is a DEXA scan to rule out osteoporosis (Cornelia de Lange Syndrome Foundation, 2010b).

**Case Studies**

A few case studies have been conducted to find the cause of CdLS, whether it be a gene mutation or an anomaly. Until a few years ago, the syndrome was thought to be sporadic. But recently, there has been a connection to the Nipped-B homolog (NIPBL) gene and CdLS. According to Park, Lee, Ki and Byun (2010), they found a male baby born in May 2009 weighing 1,840 grams at 32 weeks gestational age (See Fig. 7). They described his appearance as follows:

![Fig. 7 General appearance shows distinctive facial features, excessive body hair, and micromelia of both hands.](image)

The patient presented with cyanosis and respiratory difficulty requiring continuous positive airway pressure. No evidence of respiratory distress was noted on a chest radiograph…A physical examination revealed bushy eyebrows and synophrys, long curly eyelashes, long philtrum, downturned angles of the mouth and thin upper lips, cleft palate, micrognathia, excessive body hair, micromelia of both hands, flexion contracture of elbows and hypertonicity (p. 1821).

To analyze the gene mutation, peripheral blood samples were obtained from the patient with informed consent of the family. Results showed that there was indeed a gene mutation with NIPBL (Park et al., 2010).

Another case study was performed in order to study the behavioral phenotype of Cornelia de Lange syndrome. In this study Oliver, Arron, Sloneem, & Hall (2008) examined communication, compulsive and autistic-like behavior in CdLS patients. They accomplished this by identifying a syndrome group and a comparison group. The measures they used were the Wessex Scale, which is an informant questionnaire designed to assess social and physical abilities in children and adults, vineland adaptive behavior scales, which measure problem behavior, compulsive behavior checklist, and a childhood autism rating scale that is an observational rating scale. The findings were conclusive. “The majority (76%) of participants with Cornelia de Lange syndrome were classified as having severe and profound intellectual disability and this distribution of degree of intellectual disability is similar to that previously reported” (p. 469). Oliver et al. (2008) also stated that their study supports the assertion that individuals with CdLS may have an increased likelihood of showing autistic like behavior. They
found that individuals with the syndrome were significantly more likely to be categorized as severely autistic than those in the comparison group.

The findings of these case studies prove that more research should be done on CdLS. The results of Oliver et al. (2008), show that “compulsive behaviors might be more pronounced in this syndrome than would be predicted from the presence of other autistic impairments and this…alludes to the potential for an additional pathway to aspects of the behavioral phenotype” (p. 470). Further research should focus on the phenotypic characteristics noted in this study and their relationship with the genetic subtypes of Cornelia de Lange Syndrome.

**Conclusion**

Cornelia de Lange Syndrome is a multiple congenital anomaly characterized by distinctive facial features, upper limb malformations, and cognitive retardation. The syndrome affects the individual as well as the parents. The main distinctive features are bushy eyebrows, low set ears, flexion contractures of elbows, thin upper lips, and clinodactyly. There are treatments available to help, namely physical, speech, and occupational therapy, although regular testing is recommended. Studies are being done to be able to better understand CdLS and how to help those diagnosed with it.

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**Fig. 8** Infant with Cornelia de Lange syndrome demonstrating excessive hairiness, low set ears, and upturned nose.


