

Lesson 284: PreAnesthetic Assessment of the Patient with Cornelia de Lange Syndrome

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Needs statement

Committee opinion and audience surveys have identified the need to present, from time to time, rarely encountered diseases for which there are anesthetic implications.

Learning Objectives

At the end of this activity, the participant should be able to:

1. Recognize and describe the clinical features of Cornelia de Lange syndrome (CdLS).
2. List the major causes of mortality in patients with CdLS.
3. Discuss the treatment of CdLS.
4. Outline the current theory of CdLS pathogenesis.
5. Explain the importance of a preoperative evaluation of these patients.

6. Identify appropriate treatment of cardiac anomalies.
7. Describe appropriate anesthetic management of hypoxia and hypercapnia.
8. Discuss difficulties in managing the airway of the patient with CdLS.
9. List anesthetics that are contraindicated for the patient with CdLS.
10. Identify drugs recommended for inducing anesthesia in the patient with CdLS.

Case History

A 9-month-old girl weighing 14 kg with longstanding gastroesophageal reflux disease was scheduled for surgery for Nissen fundoplication. She was diagnosed with CdLS, and recently had a cardiac evaluation that did not reveal any abnormalities. All laboratory test results were within normal limits.

Cornelia de Lange syndrome (CdLS), also known as Brachmann-de Lange syndrome, is a disorder comprising multiple congenital anomalies of variable severity. It is a rare syndrome—the prevalence is estimated at 1 in 10,000 to 30,000—that is genetically heterogeneous and sporadic. First described by the Dutch pediatrician Cornelia de Lange as a diagnostic entity in 1933, isolated cases in severely affected infants had been reported separately by a Dutch anatomist Dr. Vrolik in 1849, and a German physician Dr. Brachmann in 1916.

CdLS is best characterized by a distinctive facial appearance, prenatal and postnatal growth deficiency, psychomotor delay, and upper limb malformations. Although almost all the organ systems can be affected, individuals with CdLS most notably display developmental deficits in neurosensory, craniofacial, musculoskeletal, cardiac, and gastrointestinal systems. There is no known cure, but the syndrome can be managed by treating associated clinical symptoms. In infants diagnosed with CdLS, 66% die before reaching 1 year of age.¹ Primary causes of mortality are aspiration (in infants) and infection and bowel obstruction (post-infancy).¹

Pathogenesis

Several genes have been discovered in CdLS (NIPBL, SMC1A, SMC3), all of them involved in sister-chromatid cohesion. Cohesion proteins are involved in chromosome segregation, regulation of gene expression, DNA repair, and maintenance of genome stability. Mutations in NIPBL on chromosome 5 account for about 60% of cases of CdLS, whereas mutations in SMC1A on the inactivated X chromosome, and in SMC3 on chromosome 10 account for about 5%.²

NIPBL and SMC3 mutations are both believed to be inherited in an autosomal dominant pattern. Although SMC1A mutations are believed to have an X-linked dominant pattern of inheritance, males and females are affected similarly. The genotype–phenotype correlation reveals that mutations in NIPBL result in more severe phenotypes than mutations in the SMC1A and SMC3 genes.² Moreover, the associated phenotype in NIPBL mutations increases in severity as the severity of the mutation increases.

More severe cases of CdLS develop with NIPBL deletions or truncations, whereas milder forms of the disorder occur in patients with NIPBL missense mutations. Mutations in the SMC1A and SMC3 genes are predominantly missense and small in-frame deletions. The phenotype of patients with SMC1A and

SMC3 mutations is milder, consisting mainly of mild to moderate mental retardation, and without associated severe retardation in growth and limb or systemic involvement.^{3,4} Although mutations in the 3 genes described are implicated in 65% of patients with CdLS, the pathogenesis of most cases is sporadic with a dominant pattern of inheritance.²

Clinical Manifestations

A diagnosis of CdLS is based on clinical signs and symptoms outlined in Table 1.

Table 1. Diagnostic Criteria for Cornelia de Lange Syndrome

Criteria Requirements by Body Category	<p>Facial: Synophrys (arched, fine eyebrows) <i>and</i> >3 of the following: long eyelashes; short nose, anteverted nares; long, prominent philtrum; broad or depressed nasal bridge; small or square chin; thin lips, downturned corners; high palate; widely spaced or absent teeth</p>
	<p>Growth: >2 of the following: weight below fifth percentile for age; height or length below fifth percentile for age; OFC below second percentile for age</p>
	<p>Development: >1 of the following: developmental delays or mental retardation; learning disabilities</p>
	<p>Behavior: >2 of the following: attention deficit disorder ± hyperactivity; obsessive-compulsive characteristics; anxiety; constant roaming; aggression; self-injurious behavior; extreme shyness or withdrawal; autistic-like features</p>
	<p>Musculoskeletal: Reduction defects with absent forearms (alone); or small hands and/or feet (below third percentile) <i>or</i> oligodactyly <i>and</i> >2 secondary criteria; <i>or</i> none of these <i>and</i> >3 secondary criteria</p> <p>Secondary criteria: fifth-finger clinodactyly; abnormal palmar crease; radial head dislocation/abnormal elbow extension; short first metacarpal/proximally placed thumb; bunion; partial 2,3 syndactyly toes; scoliosis; pectus excavatum; hip dislocation or dysplasia</p>
	<p>Neurosensory/skin: >3 of the following: ptosis; tear duct malformation or blepharitis; myopia, -6.00 D; major eye malformation or peripapillary pigmentation; deafness or hearing loss; seizures; cutis marmorata; hirsutism, generalized; small nipples and/or umbilicus</p>
<p>Other major systems: >3 of the following: gastrointestinal malformation/malrotation; diaphragmatic hernia; gastroesophageal reflux disease; cleft palate or submucous cleft palate; congenital heart defect; micropenis; hypospadias; cryptorchism; renal or urinary tract malformation</p>	

Diagnosis: a positive mutation on CdLS gene testing; *or* facial findings and criteria met from 2 of the growth, development, or behavior categories; *or* facial findings and criteria met for 3 other categories, including 1 from growth, development or behavior, and 2 from the other categories. Adapted from reference 6.

D, diopters; OFC, occipitofrontal circumference

Craniofacial

Facial anomalies are the most distinctive clinical feature. The head is microcephalic, with a low hairline on the forehead and posterior neck. The eyebrows are confluent and well defined, extending down to the nasal ridge and highly arched in 98% of patients.⁵ The eyelashes are thick and long, and the upper and lower lashes both exhibit an exaggerated curvature. Hypertelorism and an antimongoloid slant of the eyes are also noted. The mid-face has a flattened appearance with a short nose and anteverted nares. The nasal bridge is usually broad or depressed. The philtrum is long, smooth, and prominent, and the lips are thin with

downturned corners. Micrognathia or a square chin with a highly arched palate and cleft palate are observed in 30% of patients.⁵ Dental anomalies include widely spaced small teeth, absent teeth, and crowded teeth. The ears are set low and posteriorly rotated, and are often hirsute.

Cardiovascular

The incidence of congenital heart disease in patients is between 20% and 30%, compared with a rate of 0.8% for all births.⁵ The most common abnormalities include (in descending order of prevalence) ventricular septal defects, atrial septal defects, pulmonic stenosis, tetralogy of Fallot, hypoplastic left heart syndrome, and tricuspid aortic valve. Signs and symptoms of some heart defects are obvious at birth, prompting evaluation by a pediatric cardiologist. Because other defects are subtle and not always recognized immediately, detection of congenital heart disease in the patient with CdLS may be delayed. It is recommended that every patient with CdLS be evaluated by echocardiography.

Musculoskeletal

Along with distinctive craniofacial features, specific findings involving the extremities help establish a diagnosis. Although involvement of the lower extremities is less common than upper extremity malformations, more than 80% of those with lower extremity malformations have partial syndactyly of the second and third toes.⁵ The hands and feet are small in more than 90% of cases, and more than 50% of patients have a single palmar crease.⁵ Clinodactyly of the fifth finger is observed in 74% of cases, as well as bradydactyly.⁵ The first metacarpal usually is disproportionately shortened with a proximally placed thumb.⁶ Upper extremity malformations, observed in up to 30% of patients, range from oligodactyly to ulnar deficiency to absent forearm, with digit(s) present distal to the elbow.⁶ Other common musculoskeletal findings include radial head dislocation with abnormal elbow extension, clubbed feet, poikilothermia, pectus excavatum, scoliosis, and hip dislocation or dysplasia.

Gastrointestinal

Gastroesophageal reflux disease (GERD) is the most common gastrointestinal complication, with more than 90% incidence.⁶ Esophagitis, aspiration, chemical pneumonitis, and irritability are complications of GERD that can be avoided by diagnosis and treatment in the neonatal period. Pyloric stenosis has been reported, and may contribute to malnutrition and poor weight gain in newborns. Malrotation, observed in at least 10% of cases, is associated with an increased risk for volvulus.⁶ Congenital diaphragmatic hernia is also observed; however, the reported incidence varies and may be underestimated secondary to infant deaths in the perinatal period.

Genitourinary

Up to 40% of patients with CdLS have structural anomalies of the kidney and urinary tract; the most commonly observed are vesicoureteral reflux, pelvic dilation, and renal dysplasia with possible deficient renal function.⁶ Malformations of the genitalia also have been reported. Cryptorchism is seen in up to 73% of males, and hypoplasia and micropenis in 57%; hypospadias also is observed.⁶ Females may have small labia majora and an abnormally formed uterus.

Auditory and Vision

Up to 60% of patients have hearing loss, including both sensorineural and conductive.⁶ The ear canals are narrow—possibly stenotic—which pre-disposes these patients to otitis media and sinusitis.⁶ The most common ophthalmologic findings are peripapillary pigmentations, high myopia, ptosis, microcornia, and blepharitis. Rare ophthalmologic findings include nasolacrimal duct obstruction, nystagmus, cataracts, and glaucoma.

Neuropsychiatric

The behavioral problems of patients with CdLS are speculated to be secondary to frustration from an inability to communicate. Many individuals demonstrate behavior consistent with depression and attention-deficit/hyperactivity disorder; they also can display obsessive-compulsive behavior and autistic behavior, including self-destructive tendencies, defiance, extreme shyness, and avoidance of social interactions.

Growth and Developmental Retardation

A failure to grow occurs in more than 95% of patients with CdLS.⁶ A proportionately small stature begins prenatally—although it appears most significant by 6 months of age—and continues throughout life. Although the growth of patients with CdLS parallels standard growth curves, mean height and weight remain below the fifth percentile.⁶ Developmental delay is observed in more than 95% of patients⁶; those with classic CdLS experience profound to severe developmental delays. Overall, IQ ranges from below 30 to 102, with an average of 53.^{7,8} Patients with a mild form of CdLS have higher functioning with IQs ranging from normal to borderline with learning disabilities.⁹ Most individuals, however, experience disabilities in speech and language.

Anesthetic Considerations (Table 2)

Table 2. Anesthetic Considerations in Cornelia de Lange Syndrome

Anomalies, Contraindications	Risks, Treatments
Cardiac anomalies	Provide endocarditis prophylaxis
Pulmonary anomalies	Increased risk for respiratory infections, irritable airway, hypoxia, and hypercapnia
Renal dysfunction	Dose drugs renally
Airway	Risk for aspiration, and occlusion of airway; prepare for difficult intubation
Contraindicated drugs	Halothane and nitrous oxide
Malignant hyperthermia	Associated with paralysis in the presence of strabismus
Recommended induction agents	Sevoflurane, isoflurane, ketamine, etomidate, opioids

Pharmacology

Patients often require general anesthesia because of non-cooperative and hyperactive behavior. However, perioperatively, sedation should be administered lightly because of possible upper airway obstruction and an unpredictable response to drugs secondary to endocrine disorders.¹⁰ In cases in which the rapid induction of anesthesia is necessary, ketamine or etomidate often is recommended based on an effect of limited cardiac depression.¹⁰

In patients with suspected or confirmed pulmonary hypertension, the administration of inhaled anesthetics and opioids is recommended.¹⁰ Desflurane and sevoflurane allow for faster recovery; nitrous oxide should be avoided because it can increase pulmonary vascular resistance.¹⁰ Additionally, the induction of paralysis in patients with strabismus warrants caution because of the reported association between succinylcholine and malignant hyperthermia.¹⁰

Cardiorespiratory

A preanesthetic examination to assess for cardiorespiratory derangement is important, and often difficult. Many patients present with previously undiagnosed congenital cardiac anomalies—including tetralogy of Fallot, pulmonary or aortic stenosis, atrial or ventricular septal defect, pulmonary ductus arteriosus, hypoplasia of the left ventricle, and abnormal electrocardiographic findings (ie, atrioventricular block, and left or right ventricular hypertrophy)—discovered during anesthetic management. Cases have been reported of right bundle branch block (with and without murmur) that was initially observed during anesthetic management.¹⁰

When the presence of any such cardiac anomaly is confirmed, prophylactic administration of antibiotics is necessary against endocarditis.¹⁰ Postoperatively, complications can include unstable cardiac function and a marked susceptibility to infections. Patients who repeatedly experience episodes of upper airway obstruction secondary to macroglossia and micrognathia, in addition to cardiac anomalies, may develop pulmonary hypertension; in such cases, anesthesia may be complicated by the development of hypoxia and hypercapnia.¹⁰ Perioperatively, the successful management of these patients may include increased FiO₂ to achieve adequate oxygen saturation; the administration of prostaglandins, and even nitric oxide, may also be warranted.¹⁰

Pulmonary hypoplasia and lobular anomalies predispose patients with CdLS to respiratory infections. The most common causes of death in such patients are acute pneumonia and bronchitis.¹¹ The airway is considered to be irritable and the administration of IV hydrocortisone has been shown to relieve asthma-like symptoms that may develop during general anesthesia.¹¹

Renal/Endocrine

Endocrine disorders and renal dysfunction secondary to immaturity and malformation necessitate an evaluation of the patient to assess renal function and prepare for potential postoperative complications. A careful determination should be made of dosages for any administered drugs that are excreted by the kidney.

Airway

Serious challenges in anesthetic management may result from aspiration complications and difficult intubation secondary to the craniofacial anomalies that characterize CdLS. The risk for aspiration secondary to GERD can be managed by premedication—including famotidine, metoclopramide, and/or sodium bicarbonate—and rapid-sequence induction with succinylcholine (only in patients who do not have strabismus).

The intubation of patients with CdLS almost always requires a tube of a smaller size than that which is age-appropriate because of the immature development of airway structures, most notably the presence of a hypoplastic larynx.¹¹ Craniofacial features that predispose to difficult intubation include macroglossia, cleft lip/palate, midface hypoplasia, high arched palate, and mandibular hypoplasia. In patients with macroglossia, the enlarged tongue fills the oral cavity, obstructing the airway and impeding visualization of the larynx.

Obstruction by the tongue also can take place in individuals with a cleft palate. In such cases, the nasal airway is obstructed if the tongue falls into the cleft; the oropharynx will be completely occluded if the tongue falls posteriorly with relaxation of the oropharyngeal musculature.¹²

In patients with midface hypoplasia, the palate is high and arched, and the nasal passages are small; thus, these individuals are primarily mouth breathers—a potential problem during mask ventilation.¹² When the mouth is closed, the tongue occludes the small oral cavity and the small nasal passage creates resistance to nasal airflow. This can be overcome by holding the mouth open during induction.¹² Craniofacial dysostosis causes difficulties in mask fitting; therefore, maintaining a good mask seal is paramount.¹²

In mandibular hypoplasia the anterior mandibular space is decreased, thereby decreasing the space into which the tongue is displaced during laryngoscopy, and making tracheal intubation more difficult.¹² Patients with this condition should be managed using fiber-optic intubation, video laryngoscopy, or another advanced airway technique. In general, difficult intubations encountered in CdLS are best managed by having an introducer, laryngeal mask, or fiber-optic bronchoscope readily available.

A laryngeal mask airway is recommended as an alternative to mask ventilation or tracheal intubation, and as a tool in fiber-optic scope–assisted tracheal intubation.¹³ A laryngeal mask airway is also beneficial because no paralysis is required; this may be relevant in patients with strabismus, which can be associated with malignant hyperthermia.¹³ Some published studies advocate the application of corticosteroids before intubation to prevent airway trauma and edema in case of multiple attempts at intubation.¹⁴

Management of the Case Presented

The patient was identified as being at high risk for GERD and CdLS. Prophylactic famotidine, metoclopramide, and ondansetron were administered because of the high risk for aspiration. After a review of the patient's medical history and a physical examination emphasizing the head, neck, lungs, and heart, it was determined that the airway could be secured with a rapid-sequence induction using etomidate and succinylcholine. A 4.5-mm (internal diameter) endotracheal tube did not pass easily; a 4.0-mm endotracheal tube was inserted without trauma. Blood loss was minimal and extubation of the

trachea was accomplished in the operating room. On day 3, the patient was discharged without complications.

Conclusion

Although specific gene mutations can be found in some patients, genetic testing is usually reserved for confirming a CdLS diagnosis that is highly suspected. At present, there is no cure for CdLS. Treatment is symptomatic and therapy-based. Early intervention comprising medical and surgical care is necessary for feeding difficulties, congenital heart disease, and urinary, auditory, and visual abnormalities, as well as psychomotor delay. In summary, the anesthetic care of the patient with CdLS is often challenging; well-planned perioperative care can potentially reduce morbidity and mortality.

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REFERENCES

1. Sargent WW. Anesthetic management of a patient with Cornelia de Lange syndrome. *Anesthesiology*. 1991;74(6):1162-1163.
2. Revenkova E, Focarelli ML, Susani L, et al. Cornelia de Lange syndrome mutations in SMC1A or SMC3 affect binding to DNA. *Hum Mol Genet*. 2009;18(3):418-427.
3. Deardorff MA, Kaur M, Yaeger D, et al. Mutations in cohesin complex members SMC3 and SMC1A cause a mild variant of Cornelia de Lange syndrome with predominant mental retardation. *Am J Hum Genet*. 2007;80(3): 485-494.
4. Musio A, Selicorni A, Focarelli ML, et al. X-linked Cornelia de Lange syndrome owing to SMC1L1 mutations. *Nat Genet*. 2006;38(5):528-530.
5. Jackson L, Kline AD, Barr MA, Koch S. de Lange syndrome: a clinical review of 310 individuals. *Am J Med Genet*. 1993;47(7):940-946.
6. Kline AD, Krantz ID, Sommer A, et al. Cornelia de Lange syndrome: clinical review, diagnostic and scoring systems, and anticipatory guidance. *Am J Med Genet A*. 2007;143A(12):1287-1296.
7. Kline AD, Stanley C, Belevich J, Brodsky K, Barr M, Jackson LG. Developmental data on individuals with the Brachmann-de Lange syndrome. *Am J Med Genet*. 1993;47(7):1053-1058.
8. Saal HM, Samango-Sprouse CA, Rodnan LA, Rosenbaum KN, Custer DA. Brachmann-de Lange syndrome with normal IQ. *Am J Med Genet*. 1993;47(7):995-998.
9. Moeschler JB, Graham JM Jr. Mild Brachmann-de Lange syndrome: phenotypic and developmental characteristics of mildly affected individuals. *Am J Med Genet*. 1993;47(7):969-976.
10. Corsini LM, De Stefano G, Porras MC, Galindo S, Palencia J. Anaesthetic implications of Cornelia de Lange syndrome. *Paediatr Anaesth*. 1998;8(2):159-161.
11. Takeshita T, Akita S, Kawahara M. Anesthetic management of a patient with Cornelia de Lange syndrome. *Anesth Prog*. 1987;34(2):63-65.
12. Nargozian C. The airway in patients with craniofacial abnormalities. *Paediatr Anaesth*. 2004;14(1):53-59.
13. Fernández-García R, Pérez Mencía T, Gutiérrez-Jodra A, López García A. Anesthetic management with laryngeal mask in a child with Brachmann-de Lange syndrome. *Paediatr Anaesth*. 2006;16(6):698-700.
14. Küçükyavuz Z, Özkaynak Ö, Tüzüner AM, Kılınç R. Difficulties in anesthetic management of patients with micrognathia: report of a patient with Stickler syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102(6):e33-e36.

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Post-test

- 1. Which statement is true regarding Cornelia de Lange syndrome (CdLS)?**
 - a. The diagnosis is based on clinical signs and symptoms.
 - b. The diagnosis does not require the presence of craniofacial abnormalities.
 - c. It is associated with a 5% incidence of mortality in the first year of life.
 - d. The estimated prevalence of the disorder is 1 in 5,000.

- 2. Mortality in infants with CdLS is a result of:**
 - a. bowel obstruction
 - b. endocarditis
 - c. pneumonia
 - d. aspiration

- 3. The most distinctive clinical anomaly in CdLS is:**
 - a. craniofacial features
 - b. gastrointestinal malrotation
 - c. developmental delay
 - d. fifth-finger clinodactyly

- 4. Which statement is true regarding halothane?**
 - a. It is not recommended for patients with CdLS.
 - b. It allows for faster patient recovery than sevoflurane.
 - c. It is usually associated with malignant hyperthermia in patients with CdLS.
 - d. It is the recommended induction agent in patients with CdLS.

- 5. If a cardiac anomaly is confirmed in a surgical patient with CdLS, the clinician should:**
 - a. administer antibiotics for endocarditis prophylaxis
 - b. cancel the surgery
 - c. do nothing
 - d. perform echocardiography before and after the operation

6. The placement of a supraglottic airway in the patient with CdLS:

- a. is recommended as an alternative to mask ventilation
- b. is not recommended in the presence of strabismus
- c. requires a size larger than that which is age-appropriate because of macroglossia
- d. is not recommended

7. The pathogenesis of CdLS is:

- a. unknown
- b. sporadic and involves a recessive pattern of inheritance
- c. involves autosomal dominant mutations in NIPBL, SMC3, and SMC1A genes
- d. sporadic and involves a dominant pattern of inheritance

8. Clinicians should be aware of which postoperative complication(s) in the patient with CdLS?

- a. Unstable cardiac function
- b. Increased risk for infection
- c. Respiratory instability
- d. All of the above

9. Which statement is true regarding respiratory disorders in patients with CdLS?

- a. The disorders include pulmonary hypoplasia and lobular anomalies.
- b. Patients with such disorders are predisposed to respiratory infections.
- c. Such disorders can be fatal, secondary to acute pneumonia and bronchitis.
- d. All of the above

10. The use of which pharmacologic agent is contraindicated in the presence of pulmonary hypertension?

- a. Sevoflurane
- b. Isoflurane
- c. Nitrous oxide
- d. Opioids