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A Patient with Cornelia De Lange Syndrome

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A PATIENT WITH CORNELIA DE LANGE SYNDROME

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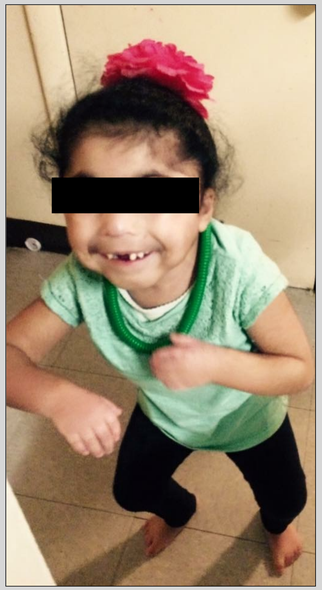
INTRODUCTION

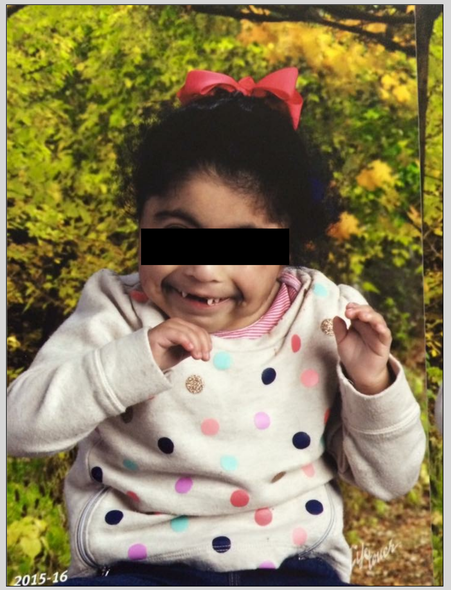
Cornelia De Lange Syndrome (CdLS) is a rare genetic condition with many distinct anomalies that can potentially cause a challenge to anesthetic management.

CASE DESCRIPTION

A six year old female with a history of CdLS presented for bilateral hamstring lengthening. She was non-verbal, developmentally-delayed and presented with the craniofacial anomalies that are associated with CdLS. She was born pre-term with a moderate ventricular septal defect which resolved without surgical intervention. Her medical history was also significant for pulmonary stenosis, and significant gastroesophageal reflux disease (GERD). She also had a known history of difficult intubations. Following an inhalational induction, a difficult intravenous line was placed. Her airway was secured with a laryngeal mask airway and spontaneous ventilation was maintained. She had an uneventful intra-operative course without any postoperative complications.



Note the short stature, limb anomalies and craniofacial anomalies associated with CdLS . (Photo provided by family of subject).



Note the craniofacial features unique to CdLS, including the flattened midface, widely-spaced teeth, excess hair, and confluent eyebrow. (Photo provided by family of subject).

DISCUSSION

CdLS is a rare genetically heterozygous and sporadic syndrome with a prevalence of 1 in 10,000 - 30,000.[4] It is characterized by distinctive facial features and a wide range of cardiac, gastrointestinal, developmental, neuropsychiatric and musculoskeletal anomalies. This syndrome can either be autosomal dominant of inheritance or X-linked dominant pattern of inheritance depending on the specific gene mutation. Approximately 60% of cases are due to a mutation of the NIPBL gene, autosomal dominant of inheritance.[6] Other gene mutations (10%) associated with this syndrome are SMC1A (X-linked), SMC3(autosomal dominant) , HDAC8 (X-Linked), and RAD21 (autosomal dominant).[6] The proteins produced by these genes are associated with the function of the cohesin complex which plays a direct role in early development. This complex helps regulate the structure and organization of chromosomes, stabilize the cell's genetic information and repair damaged DNA.[4] However, the specific gene involved in the genetic mutation causes a wide spectrum of characteristics. SMC1A, RAD21, SMC3 are all associated with mild symptoms when compared to a mutation to the NIPBL gene.[4] In a study of 120 subjects, 47% were found to have a mutation involving NIPBL.[3] Multiple types of mutations were identified including missense, splice site, nonsense and frameshift; these different genetic mutations correlated with a spectrum of phenotypes.[3]

CONCLUSION

Cornelia de Lange Syndrome is a genetic disorder in which associated anomalies present unique challenges to anesthetic management.

Craniofacial Features Associated with Cornelia De Lange Syndrome [1,2,4-6]

- Flattened Mid-Face
- Short Stature
- Macroglossia
- Micrognathia
- Square Chin
- Cleft palate
- Low Set Ears
- Wide Spaced Teeth
- Confluent eyebrows
- Low hairline
- Long Thick Eyelashes
- Hirsutism

Anesthetic Concerns[1, 3-6]

- Pre-operative Anxiety : Hearing Loss, Developmental Delay, Non-Verbal, Tendency to self-harm [5]
- Difficult Airway:
  - Craniofacial abnormalities
  - Even though a difficult intubation is a concern and anticipated, in a retrospective analysis of 42 patients, only one patient had a difficult intubation .[1]
- Congenital Cardiac Anomalies : VSD, ASD, Pulmonary Stenosis, Tetralogy of Fallot, Hypoplastic Left Heart Syndrome
- Difficult Intravascular Access
- Aspiration risk: Gastrointestinal anomalies (GERD, intestinal malrotation, pyloric stenosis)[3]
- Seizures [4]
- Increased Susceptibility to infections [4]

References

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3. Gillis LA, McCallum J, Kaur M, et al. *Am J Hum Genet*. 2004; 75(4):610-623.
4. U.S. National Library of Medicine Web site. NIH. Genetic Home Reference: Your guide to understanding genetic conditions. https://ghr.nim.nih.gov/condition/cornelia-de-lange-syndrome . Accessed September 18, 2016.
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6. National Organization for Rare Diseases Web site. http://rarediseases.org/rare-diseases/cornelia-de-lange-syndrome . Accessed September 18, 2016.