## Title

A Pediatric Patient with Cri du Chat Syndrome and Its Anesthetic Considerations



## Journal

Proceedings of UCLA Health, 23(1)

## Authors

Ma, Christina
Zheng-Ward, Fei
Tsai, Elizabeth

## Publication Date

2019-08-09

**CLINICAL VIGNETTE**

# A Pediatric Patient with Cri du Chat Syndrome and Its Anesthetic Considerations

Christina Ma, MS4, Fei Zheng-Ward, MD and Elizabeth Tsai, MD

## *Introduction*

Cri du Chat syndrome (CdCs) is the result of a congenital cytogenetic abnormality, partial deletion of the short arm of chromosome 5 (5p-).[1,2] Approximately 1 in 15,000 to 1 in 50,000 liveborn infants are affected, most due to de novo partial deletions of 5p.[1,2] While the classic hallmark of the syndrome is the high-pitched, "mewing" cry that occurs early in life, the clinical manifestations of CdCs are heterogeneous and can affect several organ systems.[3,4] Most prominent are facial and airway dysmorphologies, including vocal cord abnormalities, microcephaly, orbital hypertelorism, downslanting palpebral fissures, and a broad nasal bridge.[1] Other characteristics include hypotonia, low birth weight and poor growth, intellectual disability and developmental delay, and, in up to 30%, congenital heart disease.[1] Each of these anatomic and functional changes may present potential challenges to the anesthetic care of patients with CdDs. We present a case of a patient with CdCs who underwent monitored anesthesia care for electroencephalogram (EEG) monitoring.

## *Case*

A 43-month-old female child with a history of jerky abnormal limb movements was admitted as an outpatient to undergo EEG monitoring to assess for infantile spasms. Past medical history included CdCs with confirmed partial deletion of the short arm of chromosome 5, global developmental delay, microcephaly, chronic lung disease, obstructive sleep apnea, and constipation. The patient was born at 36 weeks and required a 3-week stay in the NICU for feeding. Medications included budesonide and albuterol inhalation suspensions, polyethylene glycol powder, and topical ciclopirox shampoo. The patient had no known drug allergies and family history was non-contributory. Surgical history was significant for club foot repair at 3 months, with no documented problems with anesthesia administration. Review of systems was positive only for chronic cough.

On examination, vital signs were within normal limits: temperature 36˚ C, heart rate 112, respiratory rate 21, blood pressure 83/44 mmHg. The patient was underweight, measuring 88 cm and 10.7 kg, with BMI of 13.82 (5$^{th}$ percentile for age). The airway exam was limited by patient cooperation, but noted normal neck range of motion, adequate mouth opening, and midline trachea. The remainder of the physical exam was unremarkable except for bilateral rhonchi in the lungs. The patient was noted to be alert and playful. No additional laboratory tests or imaging studies were done in anticipation of the procedure.

Upon entry into the procedure room, American Society of Anesthesiology's standard monitors (EKG, non-invasive blood pressure, pulse oximetry, capnography) were attached and peripheral venous access secured with a 25-gauge IV in the left foot. The patient was positioned supine, head neutral, with pressure points padded. Warming blankets were placed. Propofol was titrated in small quantities to ensure the robustness of the EEG signals and patients comfort. The patient maintained spontaneous respirations throughout the procedure, and received 4L supplemental oxygen through face mask. The 32-minute procedure proceeded without complication and the patient successfully emerged with eye-opening and spontaneous respirations on room air. She was transported to PACU, where vital signs remained stable, before being discharged home the same day.

## *Discussion*

A number of anatomic and functional changes in patients with CdCs may present significant challenges to the safe and effective administration of anesthesia, as well as opportunities for vigilance and maintenance of safety.

**Airway**: Airway changes are thought to underlie the characteristic cat-like sound made by affected neonates and young infants. A number of morphologies have been described from a small, narrow, diamond-shaped larynx, to laryngomalacia and vocal cord paralysis, to abnormalities of the epiglottis, ranging from long and floppy to small and flaccid to hypoplastic and hypotonic.[5–8] These abnormalities can cause difficulties with ventilation and intubation. There are case reports of infants who required tracheotomy following intubation, failed tracheal intubation which required the use of a supraglottic LMA, and development of post-anesthesia obstructive apnea.[7] Furthermore, potentially limited cervical mobility and facial dysmorphologies such as microretrognathia may present additional challenges in even visualizing the airway via direct laryngoscopy.[7] To ensure maintenance of a patent airway, the anesthesiologist should prepare a variety of supraglottic airway management devices, endotracheal tubes, and laryngoscope blades. As CdCs patients age, the airway anatomy tends to normalize and the characteristic voice diminishes.[4] Our patient, who had a history of obstructive sleep apnea, was able to maintain spontaneous ventilation throughout the procedure,

which did not require general anesthesia; however, a variety of airway management devices were kept readily available in case any difficulty should have arisen.

**Hypotonia**: Many infants with CdCs are hypotonic, which may result in an intensified response to muscle relaxants.[8] Of particular concern may be hypotonia of the pharyngeal muscles, which may contribute to airway obstruction by soft tissue.[5] These potential issues should be considered while selecting muscle relaxants and pre-anesthetic medications and setting expectations for post-procedure recovery time in the PACU. Short-acting non-depolarizing neuromuscular blockers may be safer for CdCs patients. Pre-anesthetic medication may contribute to airway obstruction and should be avoided. Patients may also have an extended period of recovery time.[5,9] There are no known muscle defects caused by CdCs that could predispose to malignant hyperthermia (MH), although there is one case report from Zambia documenting probable MH, although limited hospital resources precluded definitive diagnosis.[10]

**Congenital heart disease**: Congenital heart disease (CHD), most commonly atrial and ventricular septal defects, patent ductus arteriosus, and pulmonic stenosis, affects up to 30% of CdCs patients.[5] This additional risk warrants a thorough preoperative physical examination with potential referral to a specialist for further evaluation and imaging.[9] The presence of CHD confers additional risks to anesthetic management, for example requiring the administration of additional antibiotics. Our patient did not have CHD, nor any abnormal cardiac findings on physical exam.

**Low birth weight and poor growth**: No specific endocrinopathies or disorders in metabolism have been associated with the low birth weight and poor growth that is commonly seen in CdCs patients.[2] They are more likely a result of a variety of issues, including poor feeding, chronic constipation, and frequent respiratory tract infections.[2] Care should be taken in maintaining normothermia for these children. Our patient was given warming blankets and maintained normal body temperature during the non-invasive procedure.

**Unmasked recessive conditions**: The 5p deletion can unmask recessive conditions. For example, primary ciliary dyskinesia, which results in frequent respiratory infections including sinusitis, otitis media, pneumonia, results from an autosomal recessive mutation of the DNAH5 gene.[11] This gene, located on 5p, is responsible for dynein formation. Patients with CdCs should be screened for any underlying pulmonary disease that could interfere with oxygenation during anesthesia, if there are signs and symptoms to suggest so.

### *Conclusion*

The childhood death rate of individuals affected by CdCs was reported to be as high at 9.7% in the 1970s, shortly after it was first described in 1963.[2] More recently, however, the overall reported childhood death rate is 6.4%, with a smaller percentage of mortality within the first year of life, according to statistics kept by the 5p Minus Family Database.[2] With increased early interventions such as physical and occupational therapy, prognosis has improved for these patients. Many patients with CdCs are born with conditions that necessitate procedures and surgical correction, and thus it behooves anesthesiologists to gain familiarity with traits associated with the syndrome that may present additional challenges to care. Our underweight 43-month female child safely underwent monitored anesthesia care for EEG monitoring.

## REFERENCES


1. **Mainardi PC**. Cri du Chat syndrome. *Orphanet J Rare Dis*. 2006;1:33. Available at: https://ojrd.biomedcentral.com/articles/10.1186/1750-1172-1-33.
2. **Nguyen JM, Qualmann KJ, Okashah R, Reilly A, Alexeyev MF, Campbell DJ**. 5p deletions: Current knowledge and future directions. *Am J Med Genet C Semin Med Genet*. 2015 Sep;169(3):224-38. doi: 10.1002/ajmg.c.31444. Epub 2015 Aug 3. Review. PubMed PMID: 26235846; PubMed Central PMCID: PMC4736720.
3. **Overhauser J, Huang X, Gersh M, Wilson W, McMahon J, Bengtsson U, Rojas K, Meyer M, Wasmuth JJ**. Molecular and phenotypic mapping of the short arm of chromosome 5: sublocalization of the critical region for the cri-du-chat syndrome. *Hum Mol Genet*. 1994 Feb;3(2):247-52. PubMed PMID: 8004090.
4. **Church DM, Bengtsson U, Nielsen KV, Wasmuth JJ, Niebuhr E**. Molecular definition of deletions of different segments of distal 5p that result in distinct phenotypic features. *Am J Hum Genet*. 1995 May;56(5):1162-72. PubMed PMID: 7726173; PubMed Central PMCID: PMC1801456.
5. **Brislin RP, Stayer SA, Schwartz RE**. Anaesthetic considerations for the patient with cri du chat syndrome. *Paediatr Anaesth*. 1995;5(2):139-41. PubMed PMID: 7489425.
6. **Colover J, Lucas M, Comley JA, Roe AM**. Neurological abnormalities in the 'cri-du-chat' syndrome. *J Neurol Neurosurg Psychiatry*. 1972 Oct;35(5):711-9. PubMed PMID: 5084140; PubMed Central PMCID: PMC494155.
7. **Guala A, Spunton M, Mainardi PC, Emmig U, Acucella G, Danesino C**. Anesthesia in Cri du Chat syndrome: Information on 51 Italian patients. *Am J Med Genet A*. 2015 May;167A(5):1168-70. doi: 10.1002/ajmg.a.36992. Epub 2015 Mar 28. PubMed PMID: 25820652.
8. **Yamashita M, Tanioka F, Taniguchi K, Matsuki A, Oyama T**. Anesthetic considerations in cri du chat syndrome: a report of three cases. *Anesthesiology*. 1985 Aug;63(2):201-2. PubMed PMID: 4025870.
9. **dos Santos KM, de Rezende DC, Borges ZD**. Anesthetic management of a patient with Cri Du Chat syndrome. Case report. *Rev Bras Anestesiol*. 2010 Nov-Dec;60(6):630-3, 350-1. doi: 10.1016/S0034-7094(10)70078-7. English, Portuguese. PubMed PMID: 21146059.
10. **Amata AO**. Difficult airway management and suspected malignant hyperthermia in a Child with Cri Du Chat Syndrome. *Saudi J Anaesth*. 2019 Jan-Mar;13(1):81-83.

doi: 10.4103/sja.SJA_304_18. PubMed PMID: 30692897; PubMed Central PMCID: PMC6329231.

11. **Shapiro AJ, Weck KE, Chao KC, Rosenfeld M, Nygren AO, Knowles MR, Leigh MW, Zariwala MA**. Cri du chat syndrome and primary ciliary dyskinesia: a common genetic cause on chromosome 5p. *J Pediatr*. 2014 Oct;165(4):858-61. doi: 10.1016/j.jpeds.2014.06.048. Epub 2014 Jul 25. PubMed PMID: 25066065; PubMed Central PMCID: PMC4177261.

*Submitted June 4, 2019*