

Perioperative Care of a Pediatric Patient With Cockayne Syndrome

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Abstract

First described in 1936, Cockayne is an autosomal recessive neurodegenerative disorder characterized by dwarfism, premature aging, impaired development of the nervous system, dental complications, abnormal photosensitivity, and optic atrophy. Of primary concern to anesthesiologists is the potential for a difficult airway related to many physical features including micrognathia, a small mouth, large teeth, overbite, limited mouth opening, and restriction of temporomandibular joint movement. Additional comorbid involvement includes associated coronary artery disease, hypertension, and diabetes. The perioperative implications of Cockayne syndrome are discussed, previous perioperative reports are reviewed, and options for anesthetic care are presented.

Keywords: Cockayne syndrome; Anesthesia

Introduction

Described in 1936, Cockayne syndrome (CS), also known as Neill-Dingwall syndrome, is a rare autosomal recessive neurodegenerative disorder characterized by dwarfism, premature aging, impaired development of the nervous system, dental complications, abnormal photosensitivity, and optic atrophy [1, 2]. Confirmation of the diagnosis is possible using genetic testing with the demonstration of a repair/synthesis defect of DNA/RNA in response to ultra-violet radiation in cultured fibroblast cells [3, 4]. The defective DNA repair from mutations in the excision repair cross-complementation group 6 (ERCC6) and ERCC8 may be a cause of Alzheimer neurofibrillary tangles as well as lipofuscin accumulation in neurons and calcific vascu-

lopathy which contribute to the impaired development of the central nervous system (CNS) and premature aging [4, 5]. At birth, head circumference may not be normal, but CNS growth failure results in progressive microcephaly [6]. Intracranial calcifications and dysfunction of the CNS including the basal ganglia results in cerebellar ataxia, mental retardation, and blindness [1]. The phenotypic pattern is consistent with an abnormal facies with a beak-like pointed nose, large ears, micrognathia, and a loss of subcutaneous fat around the cheeks resulting in what has been described as a “bird-like” appearance.

Additional clinical manifestations include growth retardation with failure to thrive, premature aging, type 2 diabetes mellitus, cardiovascular involvement, osteopenia, kyphosis, hair thinning, and skin atrophy [7]. Growth failure due to disproportionate dwarfism and ataxia results in a gait disorder with the majority of patients becoming non-ambulatory [1, 8-10]. Life expectancy is approximately 10 - 12 years of age, especially in patients with the early onset type of CS (see below). Given the multi-system involvement of the disorder, patients may present for surgical procedures of the airway, CNS, or the heart. We present a 5-year-old boy with CS who presented for bilateral club foot repair. The perioperative concerns of such patients are discussed and previous reports of anesthetic care are reviewed.

Case Report

Patient or parent consent for publication of a case report is not required by the Institutional Review Board of Nationwide Children's Hospital (Columbus, OH, USA). This patient was cared for during a surgical mission trip of Kids First Orthopedic Group (Nashville, TN) to San Miguel, Mexico. The patient was a 9.6 kg, 5-year-old child with CS who presented for bilateral club foot repair. CS was diagnosed during the first year of life during an evaluation for poor weight gain and abnormal facies. The patient was on no medications. There was no significant past medical or surgical history. On physical examination, the patient was noted to have microcephaly and an abnormal facies with a beak-like pointed nose, large ears, and micrognathia. He was non-verbal and ambulated only with a walker or support. Airway examination was difficult due to lack of cooperation, but revealed a Mallampati class 3 airway. The cardiovascular and respiratory examinations were unremarkable. Preoperative vital signs include heart rate (HR) of 118 beats/min, blood pressure (BP) of 84/46 mm Hg, respiratory rate of 20 breaths/min, body temperature of 36 °C, and room air

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Table 1. Summary of Previous Reports of Anesthetic Care for Patients With Cockayne Syndrome

Author and reference	Patient demographics	Outcome and anesthetic care
Cook [11]	A 9-year-old girl for dental surgery (extractions)	Inhalation induction with halothane. Bag-mask ventilation was difficult with upper airway obstruction. DL was difficult with visualization of the cords and arytenoids. ETT passed on third attempt after the administration of succinylcholine. Cricoid narrowing was noted as 5.0 and 4.5 mm ETTs could not be passed so a 3.5 mm ETT was used. No postoperative issues.
O'Brien and Ginsberg [12]	A 4-year-old girl for extraction of left lamellar cataract	Inhalation induction with halothane. DL was difficult with narrow and highly arched palate, stiff epiglottis, and immobile larynx. A 3.5 mm ETT was successfully placed. No postoperative issues.
Wooldridge et al [13, 14]	A 19-year-old male for Nissen fundoplication and gastrostomy	RSI with thiopentone and succinylcholine. DL was difficult with only tip of epiglottis visible. Several failed attempts at "blind" oral intubation using 5 mm ETT. Bag-mask ventilation was difficult even with an oral airway. LMA was inserted and a guidewire placed using FOB as a conduit for the ETT. Neuromuscular blockade maintained with a second dose of succinylcholine. No postoperative issues.
	A 2-month-old girl for bilateral lensectomies	Inhalation induction with halothane. Oral airway insertion improved bag-mask ventilation. An LMA was easily inserted with improved air exchange. On second attempt, the epiglottis was visible with a Cormack and Lehane grade III-IV view. A 2.5 mm ETT was passed behind the epiglottis "blindly".
	An 11-month-old boy for bilateral lensectomies	Inhalation induction with halothane. Larynx assessed as Cormack and Lehane grade III. A 4.0 mm ETT was passed on the first attempt "blindly" behind the epiglottis. No postoperative issues.
Yuen et al [15]	A 9-year-old girl for dental restorations	Intravenous induction with fentanyl and propofol. Easy bag-mask ventilation. A 4.5 mm ETT was placed without issues. At the completion of the case, prolonged emergence was noted. Hypertension (199/97 mm Hg) with ST depression noted.
Shimzu et al [16]	A 6-year-old girl for liver biopsy	Inhalation induction using sevoflurane. No problems with endotracheal intubation. No postoperative issues.
Rawlinson and Webster [17]	An 18-year-old female undergoing cesarean section	Spinal anesthesia with bupivacaine injected into subarachnoid space.
Raghavendran et al [18]	A 15-year-old girl for excision of posterior capsular membrane	Inhalation induction using sevoflurane. Mask ventilation straight forward. DL revealed grade 2 view of the glottis. A 4.0 mm ETT was placed. No postoperative issues.
Gaddam et al [19]	A 14-year-old male for dental restoration	Limited information regarding anesthetic care.
Tsukamoto et al [20]	A 17-year-old girl for dental treatment	Inhalation induction using sevoflurane. Easy bag-mask ventilation. A 5.0 mm ETT was successfully placed on the first attempt.

DL: direct laryngoscopy; ETT: endotracheal tube; RSI: rapid sequence intubation; LMA: laryngeal mask airway; FOB: fiberoptic bronchoscope.

oxygen saturation of 96%. The patient was held *nil per os* for 6 h for solids and 2 h for clear liquids. He was transported to the operating room and standard American Society of Anesthesiologists' monitors were placed. Anesthesia was induced by the inhalation of sevoflurane in oxygen and a peripheral intravenous catheter was placed. Bag-valve-mask ventilation was provided without difficulty. Propofol (1.5 mg/kg) was administered and a size 2 laryngeal mask airway (LMA) was placed. Following LMA placement, the patient was placed in the lateral Sims' position and a caudal epidural block was placed with the administration of 10 mL of 0.25% bupivacaine with epinephrine 1:200,000 and clonidine (10 µg). Anesthesia was maintained with 2-3% sevoflurane (inspired concentration) in oxygen with spontaneous ventilation and fentanyl (1 µg/kg). No response was noted to surgical incision and the sevoflurane was decreased to 1.5-2%. Intraoperative vital signs were sta-

ble with an HR of 110 - 140 beats/min, BP of 68 - 88/40 - 58 mm Hg, oxygen saturation of 97-100%, and respiratory rate of 18 - 24 breaths/min. The operative procedure lasted 75 min. Total intraoperative blood loss was less than 10 mL. Intraoperative fluids included 220 mL of Hartmann's solution. At the completion of the surgical procedure, the LMA was removed and the patient was transported to the post-anesthesia care unit (PACU). His postoperative course was unremarkable. He was discharged to the inpatient ward from the PACU and then home the following day. Postoperative analgesia was provided by intermittent doses of oral acetaminophen.

Discussion

There are several perioperative concerns to consider when

planning anesthetic care for patients with CS. Previous reports of anesthetic care for patients with CS are summarized in Table 1 [11-20]. As with any anesthetic care, appropriate preoperative preparation begins with a thorough history and physical examination. Of primary concern to anesthesia providers is the potential for a difficult airway related to many physical features including micrognathia, a small mouth, large teeth, overbite, limited mouth opening, and restriction of temporomandibular joint movement. The available literature clearly shows that direct laryngoscopy may be problematic and that bag-valve-mask ventilation may be difficult. In most cases of difficult bag-valve-mask ventilation, the placement of an LMA has resulted in effective gas exchange. Given these concerns, the appropriate equipment for dealing with the difficult airway including indirect video-laryngoscopy should be readily available prior to anesthetic induction [21]. General anesthesia can be induced by the inhalation of sevoflurane in 100% oxygen with the maintenance of spontaneous ventilation. The report of Tsukamoto et al suggests that the use of continuous processed electroencephalogram (EEG) monitoring with devices such as the bispectral index (BIS) may be useful as there may be discordance between the hemodynamic parameters and the depth of anesthesia from the EEG [20]. In their report, the authors noted a rapid decline of the BIS to less than 10 during the induction of anesthesia with 8% sevoflurane. The administration of neuromuscular blocking agents (NMBAs) should be avoided until adequate bag-valve-mask ventilation is demonstrated. Due to degeneration and involvement of the CNS, patients may have associated gastroesophageal reflux, suggesting that an RSI is indicated. However, given for the potential for airway difficulties, inhalation induction with the application of cricoid pressure may be preferable to RSI. The available anecdotal evidence has demonstrated that in many cases, a smaller than age-appropriate endotracheal tube (ETT) is frequently required due to the associated growth retardation and the potential for subglottic narrowing of the airway.

With the associated neurologic and muscle involvement, one of the main perioperative concerns in providing anesthetic care of such patients is the choice of NMBA. Although it provides a rapid onset of neuromuscular blockade and is often chosen for RSI or if difficulties with endotracheal intubation are anticipated, it has been suggested that succinylcholine be avoided in CS due to the associated neurologic and myopathic involvement and the potential for an exaggerated hyperkalemic response [22, 23]. In our patient, given the surgical procedure, NMBAs were not required and the airway was managed with an LMA and spontaneous ventilation was maintained. In the event that neuromuscular blockade is required for the surgical procedure, non-depolarizing NMBAs (vecuronium or atracurium) should be used with care as the effect may be prolonged even with routine dosing in patients with pre-existing neuromuscular diseases or hypotonia. Alternatively, where available, sugammadex may provide an additional margin of safety for reversal of the neuromuscular blocking effects of rocuronium or vecuronium.

Comorbid end-organ involvement with CS may also include cardiovascular, endocrine, and renal involvement. Hypertension commonly occurs as part of CS, with elevated renin levels [24]. Autopsy data have demonstrated premature cer-

bral arteriosclerosis with the potential for strokes [2, 25, 26]. Coronary artery involvement may predispose to myocardial ischemia as demonstrated by one case report of Yuen et al [15]. During perioperative care, ECG monitoring for ischemia with control of factors regulating myocardial oxygen delivery including diastolic BP and heart rate is suggested. Diabetes mellitus and renal involvement have been reported with CS. Renal biopsy specimens have revealed collapsed glomeruli with a thickened basement membrane, atrophic capillary loops, and advanced hyalinization resulting in decreased renal function [27]. As indicated, preoperative evaluation of renal function, electrolytes, and blood glucose may be indicated.

In summary, we present the anesthetic considerations of a 5-year-old boy with CS, an autosomal recessive neurodegenerative disorder characterized by dwarfism, premature aging, impaired development of the nervous system, dental complications, abnormal photosensitivity, and optic atrophy. Primary perioperative concerns include the potential for difficulties with airway management including bag-valve-mask ventilation and endotracheal intubation. Various physical features may result in problematic airway management including micrognathia, a small mouth, large teeth, overbite, limited mouth opening, and restriction of temporomandibular joint movement. Additional end-organ involvement includes progressive CNS degeneration with mental retardation, cardiovascular involvement with hypertension and accelerated atherosclerotic disease with myocardial ischemia, diabetes mellitus, and renal insufficiency. The preoperative assessment of end-organ impairment by the primary disease process, preparation for potential difficulties with endotracheal intubation, and close postoperative monitoring are suggested for the effective perioperative care of these patients.

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