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CASE REPORTS

Anesthesia management of pediatric dentistry patients with cardiofaciocutaneous syndrome: a case report

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Abstract Cardiofaciocutaneous syndrome is a rare syndrome characterized by particular craniofacial features, cardiac abnormalities, and multiple organ diseases. Patients present with pulmonary stenosis, hypertrophic cardiomyopathy, short neck, micrognathia, laryngomalacia, and tracheomalacia. These conditions may strongly influence patient perioperative outcomes. We describe a 15-year-old child with cardiofaciocutaneous syndrome presenting for a dentistry procedure. She had an uneventful perioperative and postoperative course except for difficult airway management.

Introduction

Cardiofaciocutaneous (CFC) syndrome is a rare condition characterized by an autosomal dominant inheritance pattern and several congenital abnormalities involving multiple organ systems.[1] The cardiac defects include pulmonary stenosis, atrial and ventricular septal defects, Hypertrophic Cardiomyopathy (HOCM), heart valve anomalies (mitral valve dysplasia, tricuspid valve dysplasia, and bicuspid aortic valve), and rhythm disturbances. These defects may be identified at birth or later in life.[1,2] Craniofacial inspection reveals high forehead, macrocephaly, bitemporal narrowing, hypoplasia of the supraorbital ridges, ocular hypertelorism, down slanting palpebral fissures, epicanthal folds, ptosis, short wide nose, and anteverted nares, posteriorly rotated low-set ears. Airway presents high-arched palate, relative micrognathia, laryngomalacia, tracheomalacia, and hypersalivation. Osteo-muscular malformations (kyphosis, scoliosis, hypotonia), gastroesophageal reflux, growth hormone deficit, developmental delay, and seizure disease may be displayed.[1] Currently, more than 100 individuals with CFC syndrome are reported in the literature, and 200 to 300 individuals are estimated worldwide.[1] To the best of

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our knowledge, this is the first report describing anesthesia management in dentistry procedures in a patient with CFC. Consent was obtained from the patient's parent to publish this case report. Institutional review board approval was not necessary.

Case

A 15-year-old female child presented for elective dental treatment of high-level caries. Because of her heart defect and dysmorphic facial features two years after birth, a genetic workup revealed a MEK1 gene mutation diagnostic for CFC syndrome. Her medical history was significant for seizure disorder, global development delay, gastroesophageal reflux, megacolon, and severe scoliosis. 2D color Doppler echocardiography documented asymmetric hypertrophic cardiomyopathy of the left ventricle (interventricular septum diastolic thickness of 11 mm and 15 mm in the subaortic portion), no obstruction of the Left Ventricular Outflow Tract (LVOT wave maximum velocity (V_{LVOT}) =167 $cm.s^{-1}$), mitral valve dysplasia with moderate mitral insufficiency, and ejection fraction of 62%.

On the day of surgery, her physical examination revealed an alert female with body mass index of 19. The patient had macrocephaly with narrowing at the temples, short and wide nose, hypertelorism, and low-set ears. Full airway examination was not possible because the patient was uncooperative; nevertheless, we observed macroglossia, short neck and short thyromental distance, which are predictors of possible difficult intubation. Moreover, she presented severe scoliosis with a moderate restrictive respiratory deficit.

She presented generalized hypotonia that was greater in her lower extremities. Her seizure disorder was managed with levetiracetam 250 mg twice daily, perampanel 4 mg, and carbamazepine 400 mg twice daily. After monitoring, the patient's vital parameters were as follows: arterial blood pressure 110/54 mmHg, heart rate 92 bpm, respiratory rate 21 min, temperature 36.3°C, oxyhemoglobin saturation 95% while breathing room air, and bispectral index 96. Anesthesia was induced with nitrous oxide and oxygen (7:3 ratio) and 8% sevoflurane. After insertion of an intravenous (IV) catheter, 20 mg of propofol, 20 mcg of fentanyl, and 20 mg of rocuronium were administered. Subsequently, mild airway obstruction occurred, which was easily remedied by an oropharyngeal airway and positive pressure. The first direct laryngoscopy with a number 3 Macintosh laryngoscope revealed difficult glottis visualization (Cormack-Lehane score 3). Two more attempts using Glidescope were needed to secure the patient airway. After optimizing head and neck extension, videolaryngoscopy with a number 3 angulated blade associated with BURP (Backward Upward Rightward Pressure) enhanced glottis visualization (Cormack-Lehane score 2), allowing intubation with a 4.5 mm cuffed endotracheal tube armored with a preformed stylet, without using glottis directed topical spray of lidocaine. General anesthesia was maintained with sevoflurane (1.5~2.5%) according to a bispectral index value between 40 and 60. Amoxicillin-clavulanic acid (1 g) was given before incision. An additional 20 mg of methylprednisolone was administered after prolonged airway manipulation. Then, 10 mg of esomeprazole for gastric protection, 2 mg of dexamethasone and 2 mg of ondansetron for postoperative nausea and vomiting prevention, and 200 mg of acetaminophen for postoperative pain were administered. The surgery, consisting of seven dental extractions, lasted 56 minutes. The patient was hemodynamically stable throughout the case. Once the surgical procedure was completed, anesthesia emergence operations were carried out, and postextubation stridor complicated this stage. This complication was promptly solved through the administration of high flow oxygen and nebulized epinephrine 500 mcg in 5 mL of normal saline while gently applying CPAP. The patient was discharged in the postanesthesia care unit once she was fully awake and her vital parameters were stable. She was observed for 4 hours in the postanesthesia care unit and for 5 hours in the outpatient hospital ward, and then discharged to return home.

Discussion

CFC syndrome is part of a family of syndromes, including Noonan and Costello syndromes, which have phenotypic similarities. Noonan syndrome presents similar craniofacial traits, congenital heart defects (pulmonary valve stenosis, HOCM), and fewer neurological conditions than CFC.[1] Costello patients share similar facial traits with patients with Noonan and CFC. HOCM and rhythm disturbances are displayed in Costello syndrome.[1,3] These syndromes have analogous phenotypic presentations, thus clinical diagnosis based only on clinical features is difficult. Genetic tests are needed to differentiate between the syndromes. Noonan patients have PTPN11, KRAS, SHOC2, and NRAS1 mutations. Patients with an HRASmutation have a diagnosis of Costello syndrome.[1] CFC syndrome is characterized by mutations in genes BRAF, KRAS, MEK1 (MAP2K1), or MEK2 (MAP2K2) that are part of a RAS-extracellular signal-regulated kinase pathway that has roles in cell differentiation, proliferation, and apoptosis.[1,3]

The multisystem involvement of CFC syndrome may present significant challenges during the perioperative period. The dysregulation of the RAS/Mitogen Activated Protein Kinase (MAPK) signaling pathway contributes to the craniofacial dysmorphia of normal craniofacial development.[4] Anesthesiologists should be aware that several phenotypic craniofacial, dental, and palatal abnormalities can complicate airway management. Our patient presented macrocephaly, micrognathia, reduced thyromental distance, and a short neck. These features posed concerns regarding difficult airway management and led us to plan a stepwise approach according to the Difficult Airway Society 2015. Predicted difficult airway management was confirmed during direct laryngoscopy, and endotracheal intubation was secured using an angulated blade videolaryngoscope already available in the operating room associated with laryngeal manipulation (BURP). Anesthesia providers should be aware that although visualization of the airway is superior using angulated videolaryngoscopy, an appropriate airway view will not necessarily provide easy tube insertion. Children with predicted difficult airway management are a high-risk group, and multiple tracheal intubation attempts are an important risk factor for respiratory complications.

Thus, every tracheal intubation should be treated as a critical intervention. This case study has a major limitation. To reduce the number of intubation attempts, the use of Glidescope should have been considered as a first-line option. Furthermore, fiberoptic intubation deserves special consideration. It is the gold standard for tracheal intubation in adults with predicted difficult airways. However, this method is more difficult with the narrow airway of an uncooperative pediatric patient.

Individuals with CFC syndrome may have unrecognized laryngo-tracheomalacia that can make them prone to respiratory complications. In addition to this potential risk factor, our patient underwent prolonged airway instrumentation, and despite the administration of methylprednisolone and accurate suction of blood and secretions, she underwent postextubation stridor, which ended after prompt administration of nebulized epinephrine and CPAP. The genetic mutation in this syndrome inhibits myoblast differentiation, leading to fewer myosin heavy chains and ultimately abnormal muscle fiber size and variability.[5] Respiratory muscle weakness may render these patients sensitive to the sedative and respiratory depressant effects of opioids during the postoperative period. For this reason, we administered a low dose of fentanyl encouraging local dental anesthesia performed by the surgeon. Seventy-five percent of patients with CFC will have one or more cardiac abnormalities.[2] The most common cardiac defects are pulmonary valve stenosis (45%) and HOCM (40%), which may progress with age.[1,2] Our patient presented HOCM and mitral valve dysplasia with moderate mitral insufficiency. Because HOCM epinephrine addition to local anesthetic was avoided, nebulized epinephrine was underdosed to avoid the risk of left ventricular outflow tract obstruction. Mitral valve defects make antibiotic prophylaxis for endocarditis mandatory. Accordingly, a pediatric cardiac evaluation, including echocardiogram and electrocardiogram, is recommended during the preanesthetic assessment. Almost 50% of CFC patients will have seizures, and all have significant developmental delay.[2] Our patient had developmental delay and seizure disorder that was well controlled by antiepileptic therapy. Thereafter, anesthesiologists should be prepared for potentially challenging perioperative experiences because these patients have difficulties cooperating with medical staff.

Most patients have concomitant severe feeding problems manifesting as oral aversion, gastroesophageal reflux, gastrointestinal dysmotility, intestinal malrotation, and constipation.[1] They frequently need a feeding tube and fundoplication. Given the varying severity of reflux affecting these patients, anesthesiologists must be aware of the possibility of aspiration. Gastric reflux was not present in our patient, but considering the aspiration risk, she was fasted before induction of anesthesia.

There are very few studies describing anesthesia management in CFC syndrome. In this report, the anesthesiologist was faced with cardiac, breathing and airway management difficulties, which are the most challenging. To protect patients with CFC, it is mandatory to consider their neurological status and gastrointestinal disease as these may also heavily influence perioperative outcome.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Rauen KA. Cardiofaciocutaneous syndrome. In: Pagon RA, Adam MP, Ardinger HH, Bird TD, Dolan C, Fong CT, Smith RJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 2007. p. 1993–2020. Jan 18 [Updated 2012 Sep 6].
2. Armour CM, Allanson JE. Further delineation of cardiofaciocutaneous syndrome: clinical features of 38 individuals with proven mutations. J Med Genet. 2008;45:249–54.
3. Katcher K, Bothwell M, Tobias JD. Anaesthetic implications of Costello syndrome. Paediatr Anaesth. 2003;13:257–62.
4. Goodwin AF, Oberoi S, Landan M, et al. Craniofacial and dental development in cardiofaciocutaneous syndrome: the importance of Ras signaling homeostasis. Clin Genet. 2013;83:539–44.
5. Tidyman WE, Han SL, Rauen KA. Skeletal muscle pathology in Costello and cardiofaciocutaneous syndromes: developmental consequences of germline Ras/MAPK activation on myogenesis. Am J Med Genet C Semin in Med Genet. 2011;157C:104–14.