# Anesthetic Management of a Pediatric Patient With Cardiofaciocutaneous Syndrome

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Cardiofaciocutaneous (CFC) syndrome is a rare condition characterized by congenital heart disease, craniofacial dysmorphology, and dermatological abnormalities. CFC syndrome is one of the RASopathies, a family of syndromes that also includes Noonan and Costello syndromes, all with underlying gene mutations involving the Ras/mitogen-activated protein kinase pathways. Important considerations for anesthesiologists caring for these patients include the need to evaluate for possible cardiac defects, anticipating and planning for potentially difficult airway management, and the consideration of potential weakness of the respiratory muscles. Musculoskeletal abnormalities, such as muscle weakness and decreased muscle mass, are observed in all RASopathies, but are particularly prominent in CFC syndrome. In patients with CFC syndrome who experience respiratory muscle weakness, the use of desflurane and remifentanil may aid in a faster recovery and effectively help reduce the risk of respiratory complications, such as respiratory depression, following general anesthesia because of their rapid metabolism or elimination.

**Key Words:** Cardiofaciocutaneous syndrome; RASopathy; Muscle weakness; Desflurane; Remifentanil.

Cardiofaciocutaneous (CFC) syndrome is a rare autosomal-dominant disease caused by mutations in the genes involving the Ras/mitogen-activated protein kinase pathway. The primary clinical characteristics of CFC syndrome often include congenital heart defects, craniofacial dysmorphology, dermatological abnormalities, gastroesophageal reflux, seizure, and intellectual disability.[1] Herein, we describe the anesthetic management of a pediatric patient with CFC syndrome.

## CASE REPORT

An 8-year-old male (120 cm; 22 kg; body mass index 15.3 kg/m$^2$) with CFC syndrome and intellectual disability was scheduled for dental treatment to be performed under general anesthesia because of his uncooperative nature/poor compliance. He was wheelchair bound and unable to walk because of generalized muscle weakness. He had severe feeding problems, including gastroesophageal reflux. Additionally, he had a seizure disorder that was reported upon presentation as weekly episodes of generalized tonic-clonic seizures. His reported medications included lamotrigine (100 mg/d), sodium valproate (2 g/d), nitrazepam (20 mg/d), and clonazepam (4 mg/d). Preoperative echocardiogram and electrocardiogram for cardiac evaluation were normal. Although dental malocclusion and micrognathia were noted preoperatively, a more thorough airway evaluation was not feasible because of the patient's uncooperative nature.

General anesthesia was induced by inhaled sevoflurane (5%), $N_2O$ (2 L/min), and oxygen (4 L/min). Intravenous access was then secured with a 22-gauge intravenous catheter inserted in the dorsum of the left hand. Intraoperative anesthetic monitoring included use of a pulse oximeter, 3-lead electrocardiography, noninvasive blood pressure cuff, and capnography. Mask ventilation was initially difficult, prompting the use of an oropharyngeal airway, which permitted adequate assisted spontaneous ventilation. Because

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the preoperative airway findings suggested potential difficulty with tracheal intubation, a McGrath MAC video laryngoscopy (Covidien) was electively used to visualize the vocal cords, and nasotracheal intubation was successfully performed using an uncuffed 5.0-mm internal diameter endotracheal tube placed via the right nasal cavity. Tracheal intubation was performed without any muscle relaxants, with the use of sevoflurane (3%) and a continuous infusion of remifentanil (0.3 μg/kg/min). General anesthesia was subsequently maintained with desflurane (4–5%), oxygen (1 L/min), and air (2 L/min) in addition to remifentanil (0.15–0.2 μg/kg/min). Local anesthesia was administered via buccal infiltration of the left posterior maxillary and mandibular regions using 3.6 mL of 2% lidocaine (72 mg) with 1:80,000 epinephrine (0.045 mg). The surgical procedure was completed uneventfully and the patient was extubated awake after adequate spontaneous ventilation was confirmed. No postoperative respiratory depression or seizures were noted. The patient remained calm throughout recovery and was discharged approximately 180 minutes after emergence from general anesthesia.

## DISCUSSION

CFC syndrome was first reported in 1986 by Reynolds et al[2] and by Baraitser and Patton[3]; 8 individuals were described with distinct facial features, ectodermal abnormalities, cardiac malformations, and intellectual disability. CFC syndrome is one of the RASopathies, a family of developmental disorders with overlapping phenotypic similarities; other noted RASopathies include Noonan and Costello syndromes. Gene mutations in RASopathies inhibit myoblast differentiation, resulting in fewer myosin heavy chains and eventually abnormal muscle fiber size and variability. All RASopathies present with musculoskeletal manifestations, including muscle weakness and decreased muscle mass, but they are particularly prominent in CFC syndrome.[4] Recovery from anesthesia is faster with the use of desflurane rather than other inhalation agents such as isoflurane or sevoflurane. In patients with CFC syndrome experiencing respiratory muscle weakness, the rapid elimination of desflurane effectively prevents respiratory depression. Additionally, as with all volatile anesthetics, desflurane demonstrates anticonvulsant effects and adequately suppresses refractory status epilepticus[5]; therefore, it may be effective for maintaining general anesthesia in patients with CFC syndrome who experience frequent seizures. Moreover, use of remifentanil may aid in a faster recovery and decrease the risks of prolonged respiratory depression and loss of airway patency. The presence of respiratory muscle weakness may render these patients more vulnerable to the postoperative sedative and respiratory-depressant effects of opioids; as such, the use of long-acting opioids at the end of treatment should be avoided.

This patient was managed without the use of muscle relaxants during tracheal intubation and throughout induction and maintenance of general anesthesia. None of the previous publications regarding CFC syndrome discuss the use of muscle relaxants.[6] Therefore, patients' response to muscle relaxants remains unknown. Use of nondepolarizing neuromuscular blockers would not be precluded, but they should be used cautiously with full return of muscular function ensured prior to extubation.

Moreover, micrognathia, short neck, malocclusion, tracheomalacia, and laryngomalacia are more common in patients with CFC than in the general population, thus increasing the likelihood of difficult airway management. A laryngeal mask airway that can be used while maintaining spontaneous ventilation, without the use of muscle relaxants, may be considered effective for airway management during general anesthesia in patients with CFC syndrome. However, CFC syndrome is often complicated by gastroesophageal reflux; therefore, the choice between tracheal intubation and the use of a supraglottic airway device should be made after careful consideration. In this case, the decision to intubate was made primarily to avoid pulmonary aspiration.

Although this patient had no cardiac abnormalities, approximately 75% of patients with CFC syndrome do have cardiac defects. The most commonly noted defects include pulmonary valve stenosis (45%), hypertrophic cardiomyopathy (40%), and atrial/ventricular septal defects, which may be present at or after birth.[7] As such, there may be need for antibiotic prophylaxis in patients with CFC syndrome who have heart defects. Additionally, arrhythmias are more uncommon in CFC syndrome than in Costello syndrome. However, several different types of arrhythmias have been documented, including supraventricular tachycardia, atrioventricular block, and Wolff-Parkinson-White syndrome. Therefore, a detailed preoperative cardiac examination is warranted in patients with CFC syndrome, including electrocardiography and echocardiography.

## CONCLUSION

This case highlights the importance of a thorough preoperative cardiac evaluation, airway management,

and selection of optimal anesthetic agents when providing general anesthesia to patients with CFC syndrome.

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