

Anesthesia Challenges in the Management of Freeman-Sheldon Syndrome: Report of Two Cases and Literature Review

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Freeman-Sheldon syndrome is a congenital myopathy with a reported prevalence of less than 1 per 1 million. Also known as craniocarpotarsal dysplasia, this syndrome is characterized by muscle contractures and soft-tissue dysplasia of the face, hands, and feet. The resulting musculoskeletal deformities may require multiple orthopedic, ocular, and plastic reconstructive surgeries. The anesthetic challenges include a potentially difficult airway and intravenous access, suscep-

tibility to malignant hyperthermia, and an unpredictable response to muscle relaxants. This report of the anesthetic management of 2 children with Freeman-Sheldon syndrome emphasizes the anesthetic considerations for the successful management of patients with this syndrome.

Keywords: Difficult airway, Freeman-Sheldon syndrome, laryngeal mask airway, nontriggering anesthesia.

Freeman-Sheldon syndrome (FSS) is a rare (1 in 1 million), nonprogressive or slowly progressive disorder involving the facial, limb, and respiratory muscles.^{1,2} The condition was first described in 1938 by Ernest Freeman, a British orthopedic surgeon and Joseph Sheldon, a British physician.^{2,3} Freeman-Sheldon syndrome can be caused by mutations in the *MYH3* gene. The disease may be inherited in an autosomal dominant (more frequent) or autosomal recessive manner but may occur sporadically.^{1,4,5} It has been proposed that the condition is caused by mutations in genes that encode proteins of the contractile apparatus of fast-twitch myofibers.⁵ The underlying myopathy produces weakness, increased muscle tone, or fibrosis.¹ The 3 common dysmorphic features are circumoral fibrosis leading to microstomia with pouting lips, camptodactyly with ulnar deviation of the fingers, and talipes equinovarus.^{1,4,5} Microstomia may be associated with micrognathia, a short-webbed neck with severe restriction of neck movements and kyphoscoliosis, further increasing the difficulty in airway management. Freeman-Sheldon syndrome is also known as the craniocarpotarsal dystrophy, describing the affected parts, or “whistling face syndrome” because of the pursed lips. Windmill-vane-hand syndrome and distal arthrogryposis type 2A are alternative terms.^{2,4-7} The anesthetic challenges relate to airway management, intravenous (IV) access, regional anesthesia, and positioning along with the high risk of malignant hyperthermia (MH).^{1,2,4,6,7} We describe the challenges faced during the anesthetic management of 2 patients with this syndrome along with an appraisal of related literature.

Case Summaries

• **Case 1.** A 2-year-old boy weighing 10 kg was scheduled for a bilateral inguinal herniotomy. His face was noticeably expressionless with a puckered mouth (Figure 1). Airway assessment revealed an interincisor distance of 1.5 cm and a Mallampati grade 4. The thyromental distance and neck movements were apparently normal. He had deep-set eyes with hypertelorism and low-set ears. His wrists showed ulnar deviation, and he had contractures of the fingers with no visible veins. Results of examination of the spine revealed scoliosis involving the thoracic spine. There was no history of previous anesthesia exposure. His medical history and family history were otherwise unremarkable.

He was referred to the child developmental clinic and received a diagnosis of Freeman-Sheldon syndrome. Findings of preoperative hematologic and biochemical investigations were normal. General anesthesia in combination with regional analgesia was planned, and written informed consent was obtained from his parents.

A difficult airway cart was kept ready that included a video laryngoscope (Truview PCD, Teleflex), fiberoptic bronchoscope, and an emergency tracheostomy tray. Our initial airway management plan was to use a laryngeal mask airway (LMA, ProSeal, Teleflex) as the primary airway device. Because the surgery was superficial, the LMA was deemed a suitable choice. The ProSeal LMA is a second-generation LMA with a gastric drainage port, which reduces the aspiration risk markedly. Our secondary plan was endotracheal intubation using the Truview PCD video laryngoscope, which was kept ready as a backup device in case the LMA did not work well. This

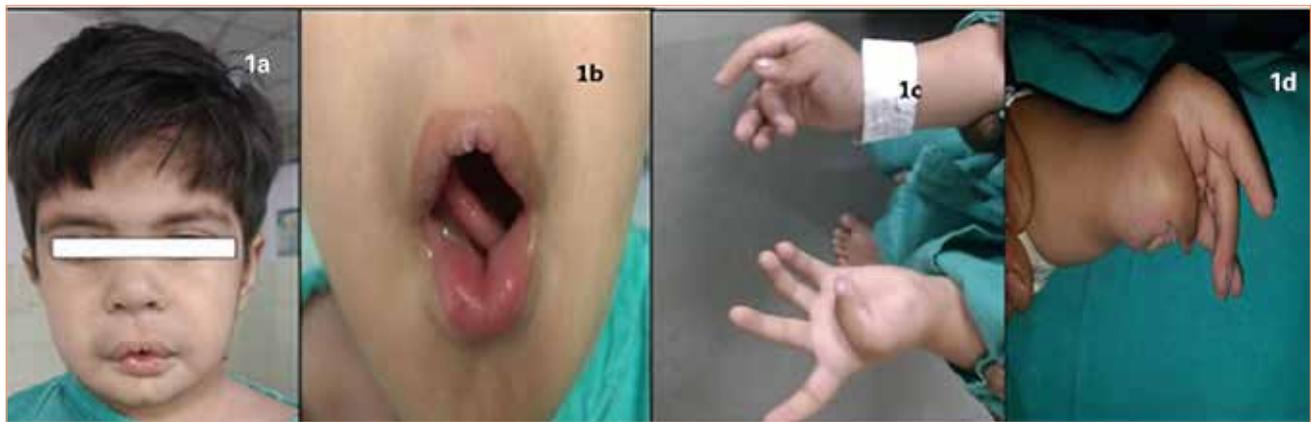


Figure 1. Case 1. A. Expressionless “whistling” facies with hypertelorism and low-set ears, common in Freeman-Sheldon syndrome. B. Airway assessment revealing mouth opening of 1.5 cm and Mallampati grade 4. C. Bilateral ulnar deviation and contractures of fingers. D. Adduction of thumb (windmill-vale-hand syndrome).

video laryngoscope is known to improve the laryngeal view in pediatric difficult airway situations, and we have been using it a long time and are comfortable with its use.

The anesthesia machine was prepared to avoid the possibility of MH. For this purpose, the system was flushed with a high fresh gas flow of 10 L/min of oxygen for 20 minutes while ventilating a breathing bag. The inhalation agent vaporizer was removed from the anesthesia system to prevent inadvertent use. The patient breathing circuit and carbon-dioxide absorbent were changed. No vein was visible in the upper limbs for cannulation. A thick layer of eutectic mixture of 2.5% lidocaine and 2.5% prilocaine anesthetic (EMLA) cream was applied to the skin over the dorsum of both feet 1 hour before IV cannulation and covered with an occlusive dressing. Routine anesthesia monitors (electrocardiogram, pulse oximeter, noninvasive blood pressure, and temperature probe) were attached to the patient. A 24-gauge IV cannula was secured over the dorsum of the left foot in a single attempt. Anesthesia was induced with IV fentanyl, 2 µg/kg, and propofol, 2 mg/kg. A lubricated, completely deflated LMA (ProSeal) size 2 was inserted with the aid of an introducer, and adequate ventilation was confirmed.

An ultrasound-guided bilateral ilioinguinal nerve block was given with 4 mL of 0.25% bupivacaine. A total of 150 mg of acetaminophen (paracetamol) was given intravenously. Anesthesia was maintained with 50% nitrous oxide (N₂O) in oxygen and a propofol infusion at the rate of 3 mg/kg/h on pressure control ventilation. Muscle relaxants were avoided. The intraoperative vital signs, including end-tidal carbon dioxide (ETCO₂) and temperature, remained stable. The 1.5-hour surgery was uneventful. The LMA was removed when the patient was awake with return of reflexes. The postoperative course was unremarkable.

• **Case 2.** A 10-month-old, 6.4-kg female infant presented with flat rockerbottom feet (Figure 2) and was scheduled for bilateral percutaneous Achilles tenotomy.

She had been given a diagnosis of Freeman-Sheldon syndrome after a genetic workup. On examination, her lips were puckered as if she were whistling, and she had a dimple in her chin. She also had microstomia and micrognathia. Her wrists showed ulnar deviation, and she had contractures of the fingers. Her ankle joints were stiff. There was a generalized increase in muscle tone. There was no history of any major medical illness or prior anesthesia exposure. Results of preoperative investigations were within normal limits.

A eutectic mixture of 2.5% lidocaine and 2.5% prilocaine anesthetic (EMLA) cream was applied on the 2 possible IV access sites on the forearms, and midazolam, 3 mg, was administered orally an hour before the child was taken to the operating room. A difficult airway cart (inclusive of a Truview PCD video laryngoscope, fiberoptic bronchoscope, and surgical airway access) was made readily available, and the anesthesia machine was prepared to avoid the possibility of MH. A 24-gauge IV cannula was secured on the right forearm in 2 attempts over the skin anesthetized with the lidocaine-prilocaine cream. Anesthesia was induced with an IV injection of 2 µg/kg of fentanyl and 3 mg/kg of propofol. Oral insertion of a well-lubricated, completely deflated size 1.5 LMA (ProSeal) fitted with an introducer was attempted without success. Another attempt was made using a 90° LMA rotation technique with an assistant applying pressure over the dorsum of the tongue using a spatula, and the LMA was successfully placed. Perioperative analgesia was supplemented via a caudal block with 5 mL of 0.25% bupivacaine and 1 µg/kg of clonidine. Anesthesia was maintained with 50% N₂O in oxygen and a propofol infusion at 4 mg/kg/h on pressure control ventilation. Muscle relaxants and inhalational anesthetics were avoided. The half-hour surgery was uneventful without signs and symptoms of MH.

The LMA was removed after the patient demonstrated spontaneous eye opening and purposeful movements. The patient was discharged home the same day.



Figure 2. Case 2. A. Bilateral congenital talipes equinovarus. B. Puckered mouth, characteristic dimple on the chin, hypertelorism, and microstomia. C. Adduction of thumb. D. Camptodactyly with ulnar deviation of fingers.

Discussion

The fibrotic nature of Freeman-Sheldon syndrome manifests with varying dysmorphic features. These patients pose several anesthetic challenges. The most obvious concern for the anesthesia provider is the difficult airway. Fibrosis of the facial muscles produce masklike faces.^{4,5,8} Perioral fibrosis (microstomia), which is barely affected by neuromuscular blockade, and restricted neck movements make laryngoscopy and intubation difficult.^{1,4} The mandibular hypoplasia, small nasal passages, and kyphoscoliosis also contribute to the challenging airway. However, microglossia and a high-arched palate have been described to aid in the proper placement of the LMA.² A characteristic dimple on the chin, hypertelorism with deep-set eyes, and short downslanting palpebral fissures are common.^{1,9} The ears may be low-set with a hearing deficit. The nasal cartilage is underdeveloped, and alae nasi are notched.¹

Microglossia and the limited movement of the soft palate cause nasal speech.⁵ Feeding problems may result from microstomia and difficulties with swallowing.^{5,10} The pharyngeal muscles may be affected, causing upper airway obstruction, gastroesophageal reflux, and aspiration.^{3,11} Patients with this syndrome are at increased risk of postoperative pulmonary complications and recurrent respiratory tract infections.^{2,5-9} The associated scoliosis and pectus excavatum may result in abnormal respiratory mechanics.^{1,11} Sleep apnea and cor pulmonale due to chronic airway obstruction have been reported.^{1,12}

The underlying myopathy may predispose these patients to MH.^{1,4,7,13} Although an association between Freeman-Sheldon syndrome and MH is not supported by a review of literature, abnormal responses to succinylcholine and halogenated volatile agents are well described.^{5,8} Unpredictable responses to neuromuscular blocking agents also increase the risk of postoperative pulmonary complications.⁷ Use of the LMA as an airway device while maintaining spontaneous ventilation with a non-MH-triggering anesthetic technique (N₂O, propofol infusion, and opioids) has been advocated in these patients.¹⁴ Nonetheless, anesthesiologists should be prepared to secure the airway with an endotra-

cheal tube in case of any emergency.

Central neuraxial block as a sole anesthetic technique can be used wherever possible in older children.^{7,15} However, associated vertebral anomalies may be considered a contraindication to central blockade. Use of peripheral nerve blocks either as a sole anesthetic technique or as a supplement to general anesthesia can minimize the use of sedatives and opioids and prevent postoperative pulmonary complications.² However, contracture and limited joint movement can make access to peripheral nerves difficult.^{2,4} Use of an ilioinguinal nerve block and caudal block in the present series helped minimize the dose requirement of the propofol infusion and enhanced postoperative recovery.

Deformed limbs with thickened subcutaneous tissues and frequent extremity surgery can result in difficult venous access, although this was not a large problem in our patients.^{1,4,5,10} Central venous access may also be difficult because of the limited movement of the short neck.

There is an association with undescended testis and inguinal hernia.^{1,4} Cardiac involvement is rare. Intelligence, general health, and life expectancy are usually normal.^{1,4}

Conclusion

Every syndrome has a unique constellation of abnormalities that could be challenging from an anesthesia provider's perspective. In a patient with Freeman-Sheldon syndrome, a potentially difficult airway, limited IV access, and a possibility of MH are the chief anesthesia concerns. Myopathy involving the respiratory muscles increases the predisposition for postoperative pulmonary complications. Use of the LMA and a nontriggering anesthesia technique using opioids and propofol infusion with or without N₂O should be considered in these patients for short procedures that do not require muscle relaxation. Regional anesthesia in the form of a neuraxial block or supplementary nerve block is particularly beneficial by reducing the requirement of sedatives and analgesics.

REFERENCES

1. Bosenberg A. Anaesthesia and Freeman-Sheldon syndrome. *S Afr J*

Anaesth Analg. October 2003;17-19.

- Patel K, Gursale A, Chavan D, Sawant P. Anaesthesia challenges in Freeman-Sheldon syndrome [letter]. *Indian J Anaesth*. 2013;57(6):632-633. doi:10.4103/0019-5049.123352
- Robinson PJ. Freeman Sheldon syndrome: severe upper airway obstruction requiring neonatal tracheostomy. *Pediatr Pulmonol*. 1997;23(6):457-459. doi:10.1002/(sici)1099-0496(199706)23:6<457::aid-ppul10>3.0.co;2-3
- Cruickshanks GF, Brown S, Chitayat D. Anaesthesia for Freeman Sheldon syndrome using a laryngeal mask airway. *Can J Anaesth*. 1999;46(8):783-787. doi:10.1007/BF03013916
- Richa FC, Yazbeck PH. Anaesthetic management of a child with Freeman-Sheldon syndrome undergoing spinal surgery. *Anaesth Intensive Care*. 2008;36(2):249-253.
- Ray S, Kirtania J, Das A, Halder B, Kundu AK. General anesthesia preceded by awake-trial of LMA in a child with Freeman-Sheldon Syndrome. *J Anesth Clin Res*. 2013;4:269. doi:10.4172/2155-6148.1000269
- Madi-Jebara S, El-Hajj C, Jawish D, Ayoub E, Kharrat K, Antakly M-C. Anesthetic management of a patient with Freeman-Sheldon syndrome: case report. *J Clin Anesth*. 2007;19(6):460-462. doi:10.1016/j.jclinane.2006.10.016
- Chen A, Lai H-Y, Lee Y, Yang Y-L, Ho J-S, Shyr M-H. Anesthesia for Freeman-Sheldon syndrome using a folded laryngeal mask airway. *Anesth Analg*. 2005;101(2):614-615. doi:10.1213/01.ANE.0000159025.99280.93
- O'Keefe M, Crawford JS, Young JD, Macrae WG. Ocular abnormalities in the Freeman-Sheldon syndrome. *Am J Ophthalmol*. 1986;102(3):346-348. doi:10.1016/0002-9394(86)90009-7
- Laishley RS, Roy WL. Freeman-Sheldon syndrome: report of three cases

and the anaesthetic implications. *Can J Anaesth*. 1986;33(3 pt 1):388-393.

- Schefels J, Wenzl TG, Merz U, et al. Functional upper airway obstruction in a child with Freeman-Sheldon syndrome. *ORL J Otorhinolaryngol Relat Spec*. 2002;64(1):53-56. doi:10.1159/000049271
- Kohyama J, Shiiki T. Sleep disordered breathing during REM sleep in Freeman-Sheldon syndrome. *Acta Neurol Scand*. 2000;102(6):395-397. doi:10.1034/j.1600-0404.2000.102006395.x
- Okawa M, Kinouchi K, Kitamura S, Taniguchi A, Sasaoka N, Fukumitsu K. Anesthetic management of an infant with Freeman-Sheldon syndrome [Japanese]. *Masui*. 2002;51(6):659-662.
- Jones R, Dolcourt JL. Muscle rigidity following halothane in two patients with Freeman Sheldon syndrome. *Anesthesiology*. 1992;77(3):599-600. doi:10.1097/00000542-199209000-00031
- Arora MK, Nagaraj G, Lakhe ST. Combined spinal-epidural anesthesia for a child with Freeman-Sheldon syndrome with difficult airway. *Anesth Analg*. 2006;103(6):786-787.

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