Treacher–Collins Syndrome with Sleep Apnea: Anesthetic Considerations

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Treacher-Collins syndrome, an incomplete form of mandibulofacial dysostosis, is a rare congenital anomaly characterized by mandibular, maxillary, and malar bone hypoplasia, bilateral deformities of auricles, lower lid defects, and antimongoloid slant of the palpebral fissures. Although Treacher–Collin's syndrome is a rare condition (incidence: 1/10,000 live births), it presents significant anesthetic and postanesthetic problems. The syndrome is associated with considerable difficulty in airway management during anesthesia; difficult, often impossible, endotracheal intubation; and occasional occurrence of obstructive sleep apnea and/or death following pharyngoplasty for velopharyngeal incompetence.[1,2] Recognition of this syndrome and its potential airway problems may prevent serious anesthetic and postanesthetic complications.

Following is a report of a petient with Treacher–Collins syndrome complicated by "sleep apnea syndrome" who was anesthetized for bilateral mandibular osteotomies and bone advancement to increase pharyngeal diameter and correct the posterior and inferior displacement of the tongue into the pharyngeal cavity.

REPORT OF A CASE

A 15-1/2-year-old, 36.5-kg, female, with Treacher–Collins syndrome complicated by obstructive sleep apnea and a seizure disorder, was scheduled for bilateral mandibular osteotomies and bone advancement. She was admitted 7 days prior to surgery for management of grand mal seizures and definitive management of progressively worsening obstructive sleep apnea. Although her obstructive sleep apnea apparently started after her posterior pharyngoplasty for velopharyngeal incompetence 22 months prior to this admission, the diagnosis was not made until 7 months later when an all-night polysomnography was done because of the development of "sleep apnea syndrome." Despite widening of nasal ports and takedown of velopharyngeal flap, the obstructive sleep apnea persisted and progressively worsened. Initially, sleep apneic episodes were brief and purely obstructive. An all-night polysomnography done 5 months prior to mandibular osteotomies and advancement, however, showed frequent and prolonged episodes of both obstructive and central apnea. With the development of grand mal seizures and severe, pathologic sleep apnea, tracheostomy was considered on admission but was refused vehemently by the patient. Because of the possibility of asphyxial encephalopathy and/or sudden death from her sleep apnea, bilateral mandibular osteotomies and bone advancement were deemed emergent.

Except for some difficulty in airway management via a mask and difficulty in endotracheal intubation, the eight general anesthetics prior to the construction of velopharyngeal flap were uncomplicated. With the onset of obstructive sleep apnea, the anesthetic and postanesthetic course in the subsequent four general anesthetics became complicated: 1) Periodic upper airway obstruction was noted with premedicant drugs resulting in excessive somnolence; 2) difficult inhalation induction of anesthesia occurred because of prolonged episodes of obstructive and/or central apnea in the somnolent stage; 3) frequent episodes of obstructive sleep apnea, followed by arousal and several deep breaths occurred in the immediate postanesthetic period; and 4) respiratory arrest and pulmonary edema occurred 40 min after a halothane–N_2O–O_2 anesthesia for tympanoplasty 1 month after posterior pharyngoplasty.

Although no premedicant drugs were given, the patient arrived in the operating room asleep, with intermittent upper airway obstruction followed by arousal and few deep breaths. Arterial blood pressure was 120/80 mmHg and heart rate of 85 bpm. She had been receiving phenobarbital 50 mg, twice daily, since admission, and had been seizure-free for 6 days; her last phenobarbital dose was given 12 h prior to anesthesia. After insertion of an intravenous line and application of appropriate monitors, atropine (0.4 mg) was administered iv and topical anesthesia of the nasopharynx (with 2 ml of 4% cocaine) and oropharynx (with 4% lidocaine aerosol spray) was done to facilitate blind nasal awake intubation and possible laryngoscopy. Although the patient was sleepy and had good topical anesthesia of the naso- and oropharynx, she became combative and resisted several attempts to pass the nasotracheal tube into the nasopharynx. Because of this, no further attempts at awake blind nasotracheal intubation were made, and the patient was given 100% oxygen via a mask and given 2.0 mg of *d*-tubocurarine iv. After giving oxygen for 2–3 min, anesthesia was induced with thiopental, 50 mg iv, followed by increasing concentrations of halothane (up to 4%) and 60% nitrous oxide. With her loss of consciousness, upper airway obstruction developed, uncorrected by an oropharyngeal airway. After a nasopharyngeal airway (26 Fr) was inserted, spontaneous, regular respiration resumed immediately. A trial laryngoscopy was performed after sufficient depth of anesthesia was attained. Since the arytenoids and posterior one-third of the vocal cords were visible with considerable external cricoid pressure, succinylcholine 60 mg, iv, was given to facilitate nasotracheal intubation. A 6-mm ID Murphy-type cuffed endotracheal tube was inserted with ease into the nasopharynx and advanced with some difficulty into the oropharynx. Laryngoscopy revealed submucosal insertion of the nasotracheal tube. Nasotracheal intubation was accomplished eventually on the second attempt after considerable manipulation of the nasotracheal tube. Anesthesia was maintained with halothane (0.5–1.0%) and 60% nitrous oxide. Her intraoperative course was uncomplicated, and with her trachea still intubated, she was taken to the recovery room awake, with no episodes of sleep apnea. Since access to the airway was limited by the intermaxillary fixation, the trachea remained intubated until the facial swelling and oropharyngeal edema had sub-

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sided. She tolerated the endotracheal tube well with meperidine, 40 mg im every 3–4 hours for pain, in addition to her usual dose of phenobarbital for her seizure disorder. Her trachea was extubated 3 days postoperatively without difficulty. An afternoon sleep apnea study done immediately after extubation showed absence of obstructive, central, or mixed apnea during REM sleep and two to three brief episodes of slight upper airway obstruction during Stage I sleep. Her postoperative course was uneventful. She has been symptom-free for almost 2 yr now (seizure-free without medication, quieter and more restful sleep, decreased nocturnal arousals, less labored breathing during sleep, and improved activity and social development).

Discussion

The narrowing of the airway in Treacher–Collins syndrome has been shown by multivideofluoroscopy, nasopharyngoscopy, and cephalometric roentgenograms (PA and lateral views) to be due predominantly to pharyngeal hypoplasia rather than retrusion of normal-sized tongue.[3] Narrowing was noted throughout the entire vertical height of the pharynx, with marked reduction in the lateral dimensions and some reduction in the anteroposterior dimensions. The pharyngeal hypoplasia is probably responsible for the difficulty in airway maintenance and endotracheal intubation and may have contributed to the development of obstructive sleep apnea, respiratory distress, and/or sudden death following posterior pharyngeal flap repair.

Obstructive sleep apnea was not evident in our patient until after the construction of the velopharyngeal flap, although she has had pharyngeal hypoplasia and glossoptosis from micro- and retrognathia since birth. The wide velopharyngeal flap and postsurgical edema may have produced considerable narrowing of the upper airway that intermittent complete upper airway obstruction occurred during certain stages of sleep. Initially, these episodes of obstruction were so brief (lasting 6–10 sec) and infrequent that the patient remained asymptomatic for months. Relief of obstruction by protrusion of the tongue, change to another stage of sleep, and/or arousal occurred as hypercapnia and hypoxia developed. As the obstructive sleep apneic episodes became more frequent and prolonged, central apnea during REM sleep and the clinical manifestations of obstructive sleep apnea became evident.

The pathogenesis of obstructive sleep apnea in patients with pharyngeal hypoplasia is not well understood; however, the role of intermittent upper airway obstruction during certain stages of sleep in the pathogenesis of this syndrome has been documented. Recent evidence indicates that this condition is due to the following sleep-related mechanisms: 1) approximation of the tongue and hypopharyngeal soft tissues during inspiration due to loss of genioglossal tone during certain stages of sleep and the negative intrathoracic pressure generated by the contraction of the diaphragm and intercostal muscles[4,5] 2) impairment of the ventilatory response to hypoxia and hypercapnia induced by the repetitive episodes of hypoxia, hypercapnia and acidosis[6]; 3) increased arousal threshold to hypoxia and hypercapnia due to alteration in the reactivity of the reticular activating system[7,8]; and 4) progressive increase in the cerebral content of gamma amino butyric acid induced by the repetitive episodes of hypoxia.[9] The disruption of CNS respiratory regulation, alteration in the reactivity of the reticular activating system, and the clinical manifestations of this condition probably are due to the CNS effects of gamma amino butyric acid.

The history is very important in identifying individuals with obstructive sleep apnea. The existence of this condition in patients with Treacher–Collin's syndrome often is missed, since these patients look normal when awake. Signs and symptoms suggestive of this problem include loud nocturnal snoring, frequent sleep arousals, abnormal motor movements during sleep, nocturnal enuresis, daytime hypersomnolence, decreased attention span and school performance, mood and personality changes, and morning headaches. Elevation of the systolic and diastolic pressures have been observed in a significant number of cases. Neurologic abnormalities are uncommon but have been reported in severe cases. Grand mal seizures may occur if the resultant hypoxia and hypercapnia are severe enough to cause cerebral hypoxia and edema.

Early recognition and immediate correction of the underlying anatomic abnormalities of the upper airway may prevent serious but preventable sequelae: cor pulmonale, failure to thrive, asphyxial brain damage, and reversible neurologic dysfunction as hypersomnolence, behavioral disturbances, and developmental delay. Management includes use of respiratory stimulants to improve ventilatory chemosensitivity while awaiting definitive management and surgical correction of the underlying upper airway abnormality: temporary tracheostomy for life-threatening obstructive sleep apnea prior to definitive management, widening of the velopharyngeal ports or takedown of velopharyngeal flap in patients with posterior pharyngoplasty, and mandibular bone advancement to increase the anteroposterior pharyngeal dimensions and anteriorly displace the hyoid bone and tongue.

The sequence of events in our patient indicates that the intermittent episodes of obstructive sleep apnea in the immediate postanesthetic period precipitated the development of acute pulmonary edema 40 minutes after an anesthetic for tympanoplasty. These episodes probably occurred because of further narrowing of the upper airway by postintubation pharyngeal and laryngeal edema, decreased genioglossal tone from the residual effects of general anesthesia,[10] and decreased ventilatory response to hypercapnia and hypoxia induced by subanesthetic concentrations of halothane[11] and morphine[12] adminis-

tered in the postanesthetic recovery room for pain. The highly negative transpulmonary pressure generated by a vigorous inspiratory effort against a totally occluded upper airway favors the transudation of fluid from the pulmonary capillaries into the interstitial space by disrupting the anatomic integrity of the capillary walls of the pulmonary microvasculature and by increasing the pulmonary vascular hydrostatic pressure.[13,14]

Awareness of the potential anesthetic problems prior to the conduct of anesthesia and careful monitoring of the upper airway in the immediate postoperative period should prevent anesthetic and postanesthetic morbidity and mortality. Anesthetic considerations include 1) possibility of prolonged episodes of upper airway obstruction in the hypersomnolent state or during sleep with use of sedatives and narcotics; 2) upper airway obstruction at subanesthetic concentrations of halothane, enflurane, and isoflurane, making inhalation induction of anesthesia and airway management by mask difficult; 3) difficult, often impossible, endotracheal intubation because of an anteriorly displaced larynx, microstomia, minimal mandibular excursion, high arched palate, and prominent maxillary teeth; and 4) possibility of pathologic obstructive sleep apnea, respiratory arrest, and acute pulmonary edema in the immediate postoperative period, especially following procedures involving the upper airway. To avoid these potential airway problems, the following guidelines should be observed: 1) narcotics, sedatives and other respiratory depressants should be avoided preoperatively and postoperatively unless the patient is carefully monitored and the airway is assured; 2) airway should be established prior to the induction of anesthesia in those cases where difficult intubation of the trachea is anticipated-awake nasal intubation, blind, or under direct vision with the use of fiberoptic bronchoscope, or tracheostomy with local anesthesia; and 3) following upper airway procedures, the trachea should remain intubated until oropharyngeal bleeding, massive soft tissue edema, or laryngeal edema have subsided.

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Erratum

The article "Effects of Intravenous or Subarachnoid Morphine on Cerebral and Spinal Cord Hemodynamics and Antagonism with Naloxone in Dogs," by Naoki Matsumiya and Shuji Dohi, ANESTHESIOLOGY, September 1983, pp. 175–181, was accepted for publication December 21, 1982, not December 21, 1983.