Anesthetic Management of a Pediatric Patient With Pfeiffer Syndrome

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Pfeiffer syndrome (PS) is a rare inherited disorder that affects the craniofacial and extremity bones but can also include anomalies of the upper and lower airways. Among the 3 subtypes, PS types 2 and 3 are the most severe. We describe the anesthetic management of a 10-year-old boy with PS type 2 scheduled for dental treatment under general anesthesia. Because of his history of Chiari malformation, avoiding neck hyperextension was recommended to prevent worsening of his neurologic function. Preoperative computed tomography revealed significant nasal stenosis but no tracheal anomalies. Considering the difficulty of nasotracheal intubation, we planned for an oral intubation. General anesthesia was induced using sevoflurane, nitrous oxide, and oxygen along with an oropharyngeal airway. After lidocaine was topically applied to the oropharynx, fiber-optic orotracheal intubation was performed under spontaneous ventilation to minimize head and neck movement. Anesthesia was maintained using desflurane and remifentanil, and no postoperative complications were observed. General anesthesia for patients with PS requires careful planning, which should include preoperative assessment of the airway to determine the feasibility of nasotracheal intubation and identify airway irregularities.

Key Words: Pfeiffer syndrome; Craniosynostosis; General anesthesia; Airway management.

Pfeiffer syndrome (PS) is a rare genetic disorder caused by specific mutations in fibroblast growth factor receptor (FGFR) genes.[1,2] PS was first described in 1964 and has an incidence of 1/100,000 neonates.[3] It most commonly involves craniosynostosis, midfacial hypoplasia, broad thumbs and great toes, brachydactyly, and variable soft tissue syndactyly.[4] Due to its clinical variability, Cohen[5] divided PS into 3 clinical subtypes based on phenotype severity: type 1 is the mildest with normal intelligence and generally has a favorable outcome, type 2 is more severe and is characterized by a trilobed or cloverleaf skull deformity, and type 3 is also more severe and is characterized by a very short skull base and severe proptosis but lacks the cloverleaf skull deformity.

When administering general anesthesia to a patient with PS, preparations for a difficult airway are necessary because maxillofacial malformations, such as nasal stenosis and related obstructive sleep apnea (OSA), are associated with upper airway obstruction. In addition, factors associated with airway obstruction in patients with PS are not limited to the midface structures but also can include lower airway/tracheal abnormalities such as tracheal stenosis and tracheal cartilaginous sleeve.[6,7] This case report describes the general anesthetic management of a pediatric patient with PS type 2 for dental treatment. Informed consent to publish the details of this case was obtained from the patient's guardian.

CASE PRESENTATION

The patient was a 10-year-old boy (height, 128 cm; weight, 28 kg; body mass index, 17.09 kg/m^2) who required general anesthesia for dental (restorative and periodontal) treatment because of intellectual disability. At birth, he had a cloverleaf skull deformity, midface hypoplasia, wide thumbs and big toes, and hydrocephalus and was subsequently diagnosed with PS type 2. The patient underwent ventriculoperitoneal shunt surgery for hydrocephalus at 4 months of age and skull enlargement surgery for premature

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fusion of the cranial sutures 1 month later. At 3 years of age, he was diagnosed with an acquired Chiari malformation and underwent foramen magnum decompression. However, partial invagination of the cerebellar tonsil into the spinal canal was still observed; therefore, his physician provided counseling on the hazards of neck bending and stretching. He experienced snoring and OSA beginning after birth and had been on continuous positive airway pressure (CPAP) until recently. He was no longer using CPAP at the time of his admission as the OSA had improved with growth, but he was still snoring and was being followed by his primary care physician.

Preanesthetic consultation revealed facial features characteristic of PS including proptosis and midface hypoplasia. No trismus was observed. Preoperative computed tomography (CT) was performed to determine the degree of nasal narrowing and identify any respiratory tract malformations, revealing significant nasal stenosis, which indicated that nasotracheal intubation would be difficult (Figure). Evaluation of the CT imaging by a pulmonologist revealed no tracheal morphology abnormalities. He had no other medical comorbidities or allergies and was not taking any regular medications.

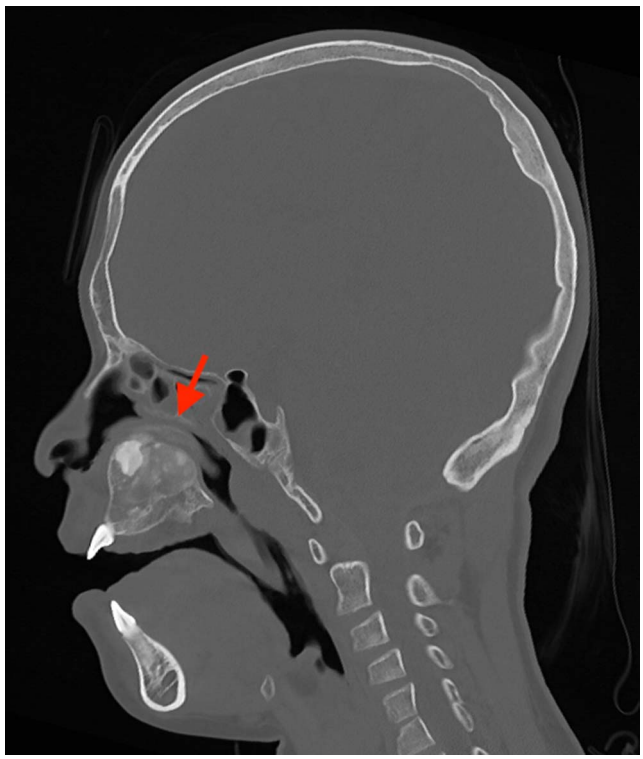
The patient's preoperative vital signs were as follows: blood pressure 105/70 mm Hg, heart rate 88 beats/min, respiratory rate 25 breaths/min, and oxygen saturation (SpO_2) 97%. There were no abnormal findings on his preoperative blood tests or on a 12-lead electrocardiogram. The patient was scheduled to undergo restorative and periodontal treatment; therefore, general anesthesia with a fiber-optic oral intubation after mask induction with spontaneous ventilation was planned.

Sedative premedication was not prescribed, and intravenous (IV) access was secured upon arrival in the operating room, after which the patient was preoxygenated (6 L/min) via face mask. General anesthesia was induced slowly with sevoflurane (5%), nitrous oxide (2 L/min), and oxygen (4 L/min). Mask ventilation was initially difficult, causing his SpO_2 to drop to 90% and prompting the use of an oropharyngeal airway, which permitted adequately assisted spontaneous ventilation. Topical anesthesia was induced by spraying 4% lidocaine around the vocal cords after administering IV atropine (0.3 mg). Movements of the epiglottis associated with spontaneous ventilation were observed using a flexible fiber-optic scope inserted through the oral cavity. Fiber-optic intubation was performed with manual neck stabilization to ensure that no anteroposterior movements occurred while securing the airway. The patient was orally intubated with a 6.0-mm ID cuffed endotracheal tube, and slight body movement was observed; however, intubation was successfully completed without any muscle relaxants using sevoflurane (3%–4%) and oxygen (6 L/min).

General anesthesia was subsequently maintained with a continuous infusion of remifentanil (0.15–0.2 μg/kg/min) and desflurane (4%), oxygen (1 L/min), and air (2 L/min). Prior to initiating the dental treatment, a pulmonologist evaluated the trachea with a fiber-optic bronchoscope, which revealed no abnormal morphology. The endotracheal tube had to be moved from one side to the other during dental treatment since the patient was orally intubated. Local anesthetics were not administered prior to dental treatment, and the patient's vital signs were stable throughout the operation.

The administration of desflurane and remifentanil was discontinued at the end of surgery. IV acetaminophen (450 mg) was administered for postoperative analgesia prior to extubation. Dental treatment was completed uneventfully, and the patient was extubated awake after adequate spontaneous ventilation was confirmed. A laryngeal mask airway was prepared as a rescue tool for upper airway obstruction following emergence from anesthesia; however, no postoperative signs of upper airway obstruction or significant oxygen desaturation were observed. The duration of surgery was 1 hour, 20 minutes, and the duration of anesthesia was 2 hour, 40 minutes. The patient was then transported to the dentistry ward, where his vital signs remained stable. He was discharged approximately 4 hours after emergence from general anesthesia, and during follow-up the next day, no problems with his general condition were observed.

Figure. Sagittal Computed Tomography View of the Head and Neck.



Significant nasal stenosis (red arrow) was identified preoperatively.

Table 1. Clinical Features of the Pfeiffer Syndrome Subtypes

Subtype	*Major characteristics*	*Other anomalies*	*Intellectual development*
Type 1	Craniosynostosis Midface hypoplasia Broad thumbs and toes Brachydactyly Variable syndactyly	Deafness Hydrocephalus	Normal
Type 2	Cloverleaf skull Proptosis Midface hypoplasia Broad thumbs and toes Brachydactyly Variable syndactyly	Hydrocephalus Cerebral or cerebellar hernia Choanal stenosis or atresia Tracheal abnormalities Ankylosis of the elbow	Developmental delay Intellectual disability
Type 3	Craniosynostosis Proptosis Midface hypoplasia Broad thumbs and toes Brachydactyly Variable syndactyly	Hydrocephalus Choanal stenosis or atresia Tracheal abnormalities Ankylosis of the elbow	Developmental delay Intellectual disability

DISCUSSION

PS is a rare autosomal dominant genetic disorder caused by mutations in the FGFR genes.[2,3] FGFRs are mainly involved in the transformation of pluripotent stem cells into osteoblasts during fetal development. Mutations in these genes can lead to prolonged protein signaling with subsequent premature fusion of the cranial bones and malformations of the extremity bones. Other syndromes related to mutations in the FGFR family include Apert, Crouzon, and Antley–Bixler syndromes.[8] Based on the severity of the phenotype, PS has been divided into 3 clinical subtypes, with types 2 and 3 having more severe neurologic compromise and respiratory problems (Table 1).[5,8]

PS type 2 consists of cloverleaf skull deformity, hydrocephalus, proptosis, finger and toe abnormalities, and neurologic complications. The main neurologic consequences that arise as part of PS type 2 include developmental delay and intellectual disabilities.[9] Therefore, it is likely that general anesthesia will be required for dental treatment in these patients. The most common facial features of patients with PS type 2 are midface hypoplasia and shallow orbits caused by an underdeveloped maxilla. Maxillary hypoplasia also results in a reduction in the nasopharyngeal and oropharyngeal airway spaces.[10] This restricts the passage of air into the trachea and lungs and causes upper airway obstruction and OSA. Inverso et al.[11] reported that the prevalence of OSA in patients with PS is 72.7%.

These patients may also present with lower respiratory tract obstruction due to a rare congenital airway malformation called tracheal cartilaginous sleeve.[6,7] Acquired Chiari malformations can also occur in patients with PS type 2, with a reported incidence as high as 50%.[12] Chiari malformation is a complex syndrome in which the brainstem medulla, cerebellar tonsils, and vermis herniate throughout the foramen magnum. Chiari malformation in patients with PS appears to be an acquired and progressive condition that develops in the first months of life because of the premature fusion of the lambdoid and cranial base sutures.[12]

Anesthetic challenges in patients with PS include airway management difficulties due to anomalies of the upper and lower airways such as nasopharyngeal stenosis, tracheal cartilaginous sleeves, and OSA. Table 2 lists the airway assessment parameters of patients with PS. In addition, if a patient with PS also has a Chiari malformation, there is added risk of neurologic deterioration, such as respiratory malfunction and dysphagia, due to anteroposterior flexion of the neck during laryngoscopy and tracheal intubation.[13] In this patient, there was significant narrowing of the nasal cavity on preoperative CT, a history of snoring and OSA, and a history of Chiari malformation. Therefore, to avoid neck movement and impossible airway maintenance during induction, we planned a fiber-optic oral intubation under inhalational anesthesia while maintaining spontaneous ventilation.

Pediatric patients with PS are likely to experience perioperative upper airway obstruction, especially under bag-valve-mask ventilation after anesthesia induction.[14] Difficulty in mask ventilation was also observed in this patient, and adequately assisted spontaneous ventilation was achieved using

Table 2. Airway Assessment Parameters for Patients with Pfeiffer Syndrome

Midface hypoplasia
Nasal stenosis or atresia
Tracheal stenosis
Tracheal cartilaginous sleeve
Tracheostomy
Previous tracheostomy
Obstructive sleep apnea

an oropharyngeal airway. Transnasal techniques to secure the airway are likely difficult in patients with PS and nasal stenosis; however, oral airway devices, such as oropharyngeal airway or laryngeal mask airways, may be effective alternatives for improving and maintaining airway patency. Spontaneous ventilation was maintained during induction, and fiber-optic orotracheal intubation was successfully performed with minimal neck movement.

As described above, PS is often accompanied by nasal stenosis,[14] and the pediatric dentist in this case requested nasotracheal intubation. However, preoperative CT findings indicated that nasotracheal intubation would be difficult to perform. When performing general anesthesia for dentistry in patients with PS, it is important to thoroughly consider the necessity of nasotracheal intubation as well as the preoperative evaluation for nasal stenosis, which may include radiographic imaging. In addition, depending on the patient, it may be possible to assess the nasal cavity using a fiber-optic bronchoscope to determine whether nasotracheal intubation is feasible after oral intubation.

For patients with PS, lower airway anomalies should also be identified as they may present with lower respiratory tract obstruction due to a tracheal cartilaginous sleeve. The tracheal cartilaginous sleeve is a continuous, vertically fused cartilaginous cylinder instead of discrete cartilaginous rings.[15] This abnormality may extend from the subglottis to the carina or bronchi. The condition is often associated with craniosynostosis syndromes, such as PS, Apert, and Crouzon, and a recent paper found a 22% (19/86) prevalence of tracheal cartilaginous sleeve in a cohort with craniosynostosis syndrome.[7] Because of the rigidity of the tracheal column, there is less natural, dynamic movement associated with the normal respiratory cycle, and the ability to clear secretions may be impaired.[15]

As a child who has a tracheal cartilaginous sleeve grows, the tubelike tracheal cartilage fails to appropriately increase in size, resulting in a relatively stenotic airway. This phenomenon places patients at risk of sudden death due to tracheal occlusion. Lertsburapa et al.[16] performed a meta-analysis of all previously reported cases of tracheal cartilaginous sleeves and reported a 90% risk of death by the age of 2 years without a tracheostomy. However, diagnosing tracheal cartilaginous sleeves is difficult and often overlooked. It is usually discovered incidentally via endoscopic examination while attempting to establish the causes of persistent respiratory difficulties or by direct visualization of the trachea during tracheostomy or autopsy. Therefore, although this patient had never been diagnosed with a tracheal cartilaginous sleeve and no tracheal stenosis was observed on preoperative CT, the pulmonology recommendation was to evaluate the trachea intraoperatively as was done by the pulmonologist using a fiber-optic bronchoscope. Typical segmentation of the tracheal ring was confirmed along with the lack of any abnormal tracheal morphology. When administering general anesthesia to patients with PS, it is advisable to assess the tracheal morphology using a fiber-optic scope after tracheal intubation.

Careful planning is required during emergence from general anesthesia in patients with PS. Because of the risk of upper airway obstruction during emergence from anesthesia, we selected desflurane as it facilitates faster emergence and recovery than other inhalational anesthetics. Remifentanil is an ultra-short-acting agent and has advantages over other opioids in terms of the incidence of postoperative opioid-induced respiratory depression. Moreover, remifentanil may also aid in faster emergence. In patients with PS, desflurane and remifentanil may help reduce the risk of postoperative upper airway obstruction due to rapid emergence and recovery. A laryngeal mask airway is almost always effective for perioperative upper airway obstruction in children with PS[14]; therefore, we prepared one as a rescue tool in case of upper airway obstruction following emergence from anesthesia although it was not needed.

CONCLUSION

PS can demonstrate the potential for upper and lower airway abnormalities such as nasopharyngeal stenosis, tracheal stenosis, and a tracheal cartilaginous sleeve. Therefore, appropriate preoperative evaluation of the airway and preparing for difficult airway management should be considered. The induction of general anesthesia requires careful planning as bag-valve-mask ventilation can be difficult. Furthermore, the presence of nasal stenosis or obstruction should be confirmed preoperatively, and the necessity and feasibility of nasotracheal intubation should be considered. In patients with PS, the use of desflurane and remifentanil may aid in faster recovery and effectively reduce the risk of upper airway obstruction following general anesthesia.

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