Anesthetic considerations for a child with PHACE syndrome: a case report

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ABSTRACT

Background: Posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe syndrome (PHACE syndrome) is a rare and serious neurocutaneous disorder. Cerebrovascular and cardiac abnormalities are the most important anesthetic concerns for patients with PHACE syndrome in order to provide safe and sufficient perioperative anesthesia care.

Case Presentation: The present case discussed the anesthetic implications of an infant boy who had PHACE syndrome and presented for elective laparoscopic-assisted pull through procedure under general anesthesia.

Conclusion: Certain perioperative anesthetic implications should be considered mainly for difficult airway management that related to airway hemangiomas, abnormal cerebrovascular structure, mainly carotid arteries, involvement that affect cerebral blood flow and results in cerebral ischemia and the association of congenital cardiac disease.

Keywords: PHACE syndrome, anesthetic considerations, case report.

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Background

An association between facial hemangiomas and intracranial arterial abnormalities was unrecognized as a syndrome and had been reported in nine cases by Ramesh et al. [1]. Dr. Ilona Freidan et al. first described this association as posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe (PHACE) syndrome in 1996 [2]. PHACE syndrome is a rare neurocutaneous syndrome that indicates the association of segmental facial hemangioma with one or more of the other cerebrovascular, cardiac, and eye anomalies. Hemangioma is usually giant, plaque like segment which covers side of the face, head, scalp as well as airway, commonly subglottic area. Posterior fossa brain malformation may be present in 41% of the patients mainly with Dandy–Walker malformation. Cerebellar agenesis or hypoplasia, supratentorial malformations involve the corpus callosum, cortical brain tissue, and intracranial hemangiomas. Clinical manifestation of intracranial pathology includes seizures, developmental delay, and recurrent headaches. Arterial malformation usually involves the cerebral vasculature and may be present as agenesis, aneurysm, or occlusion of the carotid arteries and its branches. Cardiac anomalies most commonly are aortic coarctation and aberrant subclavian artery. Eye abnormalities were reported in 14%–24% of patients with PHACE syndrome, specifically microphthalmos, optic nerve hypoplasia, cataracts, and increased retinal vascularity. Endocrine anomalies, mainly hypopituitarism and hypothyroidism, were reported in patients with PHACE syndrome. Therefore, "E" in PHACE is reflected in the eye and endocrine manifestations. When ventral developmental defects are present, it is termed PHACES syndrome, where the "S" represents sternal cleft or supraumbilical raphe [1–3,4].

Usually, patients with PHACE syndrome were presented for various surgical procedures such as airway, cerebrovascular, cardiac, and dental [1,5]. Anesthesiologists faced a huge challenge in the perioperative management of patients with PHACE syndrome as it contains serious neurovascular and airway abnormalities. Anesthetic considerations for PHACE syndrome should be tailored according to the associated abnormalities.

Case Presentation

The patient was a 7-month-old boy weighing 7.6 kg with PHACE syndrome who presented with Hirschsprung disease and colostomy. He was scheduled electively for laparoscopic-assisted pull-through procedure under general anesthesia at Prince Sultan Military Medical City.

At the age of 3 months, the patient was originally diagnosed with PHACE syndrome with manifestations of large hemangiomas on the left side of the face, upper lip, scalp and left periarticular, subglottic hemangiomas, and intracranial arterial tortuosity.

The patient was a full-term product of spontaneous vaginal delivery with birth weight of 3.0 kg. Prenatal history was unremarkable. Motor milestones and development were appropriate for his age. There was no significant neurological impairment. Surgical history revealed Hirschsprung disease and laparotomy with colostomy in the first days of his life. At age of 6 weeks, he underwent a diagnostic laparoscopic biopsy that revealed negative ganglion in the upper sigmoid and positive ganglion in descending colon.

Direct laryngoscopy and bronchoscopy were performed at the age of 3 months and it showed hemangiomas in the areas of the left glossoepiglottic fold, left side of posterior pharyngeal wall, and posterior subglottic. Later, propranolol therapy was started to diminish the size of facial hemangioma. The patient developed hyperkalemia secondary to propranolol. Potassium level reached up to 7 mmol/l without significant cardiac signs and symptoms. Propranolol was stopped and hyperkalemia was treated with calcium gluconate, salbutamol nebulizer, and sodium bicarbonate ($NaHCO_3$) until it returned to a normal serum level. Propranolol was resumed by a nephrologist after 2 days and the infant was kept under monitoring. No other episode of hyperkalemia was documented after that. Hyperkalemia therapy was gradually tapered and finally discontinued after several weeks of starting propranolol treatment. There was no airway examination performed through direct laryngoscopy and bronchoscopy after completion of propranolol therapy.

Clinical examination revealed a normal vital sign that included heart rate of 105 bpm, blood pressure of 97/50, respiratory rate of 20, oxygen saturation 99% in room air, and body temperature was 36.7°C. The infant was well nourished and active. Apart from multiple facial hemangiomas, there were no dysmorphic features. Chest and cardiovascular examination were normal. There were no neurological insults. Abdominal examination revealed the right side healthy stoma.

Routine blood investigations, chest X-ray, electrocardiography (ECG), and echocardiography were within normal limits.

Magnetic resonance imaging (MRI) and angiography for head and neck showed mild posterior anomalies in the form of hypoplastic inferior cerebellar vermis with prominent fourth ventricle and retrocerebellar cyst, suggestive of Dandy–Walker variant. Mild hypoplasia of the right cerebellar hemisphere was also suspected (Figure 1).

Magnetic resonance angiography (MRA) showed numerous dilated tortuous vascular channels and prominent vascular spaces at the superficial and deep soft tissues of the left side of the lower head and upper neck related to left facial hemangioma (Figure 2). At least two prominent dilated venous channels were also observed lateral to the left common carotid artery that could represent the dilated draining venous channels. Both subclavian arteries, common carotid arteries, internal carotid arteries, right external carotid artery, both vertebral arteries, basilar artery, and both middle cerebral arteries appeared unremarkable.

He was held nil per os for 6 hours. Intravenous access was secured prior to surgery in order to facilitate good hydration and start propranolol treatment. His preoperative vital signs revealed an oxygen saturation of 97%, blood pressure of 106/65 mm Hg, and a heart rate of 122 beats/minute. He was transferred to the operating room and routine standard monitors were applied according to the American Society of Anesthesiologists' guidelines.

Anesthesia was induced with sevoflurane in oxygen and intravenous fentanyl (2 mcg/kg). Flexible fiberoptic bronchoscopy (FOB) was performed while maintaining spontaneous ventilation with the insufflation of sevoflurane via the bronchoscope. No significant abnormalities were detected. The trachea was successfully intubated with a 3.5-mm cuffed endotracheal tube (ETT). With the cuff deflated, an air leak around the ETT was noted at 25 cm H_2O. Breath sounds were equal and bilateral with positive end-tidal carbon dioxide recorded by capnography.

Anesthesia maintained with sevoflurane was 2% in a combination of oxygen and air to maintain mean

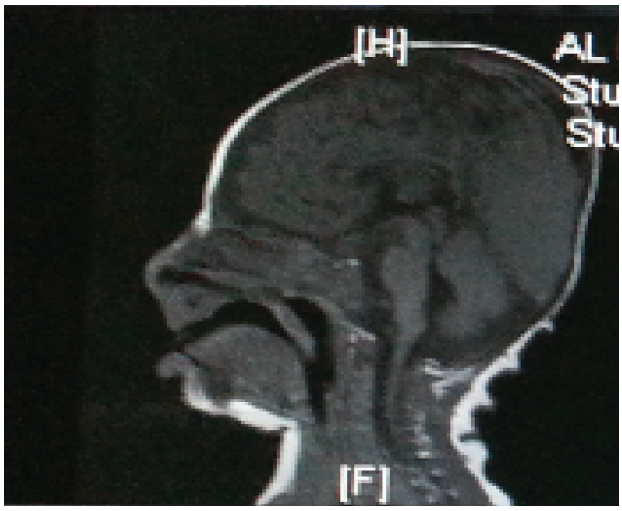

Figure 1. *Show mild posterior fossa anomalies in the form of hypoplastic inferior cerebellor vermis prominent fourth ventricle and retrocerebellar cyst suggestive of dandywalker variant.*

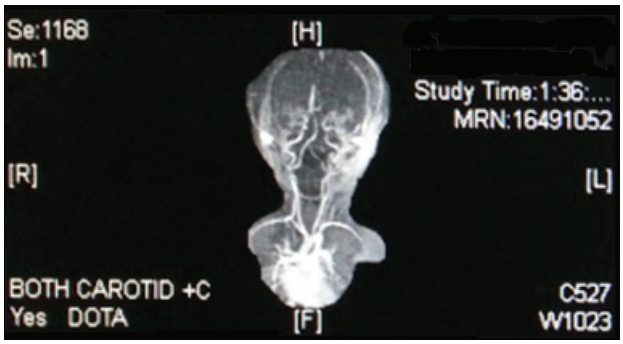

Figure 2. *MRA show dilated vascular channels.*

arterial pressure within 25% of preoperative values. Muscle relaxant in the form of cisatracurium 2 mg was given to facilitate mechanical ventilation. Caudal block was performed under complete aseptic technique with 7.5 ml of 0.2% bupivacaine and 175 mcg diamorphine. During the surgical procedure, the patient developed hyperkalemia with peak T-wave change in ECG, arterial blood gas showed potassium of 7 mmol/l. Immediate management was started with hyperventilation, calcium chloride, Ventolin inhaler, glucose, and insulin. The following blood gas showed a decrease in potassium level to 5mmol/l and T-wave in the ECG was back to normal. Estimated blood loss was 20 ml. Total intraoperative fluids were 250 ml. After completion of the surgical procedure in approximately 2 hours, the patient's trachea was extubated followed by FOB exploration to exclude airway injury. The patient was transferred to the pediatric intensive care unit for close observation and potassium level monitoring. Postoperative analgesia provided by oral acetaminophen and hydrocodone. His postoperative period was uneventful and the child was discharged from hospital on the fourth postoperative day.

Discussion

The PHACE syndrome is a neurocutaneous disorder that is newly discovered and under-recognized to the general population. It could be misdiagnosed with other disorders such as Dandy–Walker syndrome or confused with Sturge–Weber syndrome [1]. PHACE affects girls more often than boys. The female to male ratio is 8:1. Therefore, this female predominance suggests the possibility of X- linked dominant inheritance. However, the underlying pathogenesis of PHACE syndrome is still unknown and there were no reports of familial cases [1,3].

The PHACE syndrome is an acronym that stands for a combination of four major components that include segmental facial or airway Hemangiomas, Posterior fossa malformation, Arterial malformation, Cardiac anomalies, and Eye abnormalities. The term PHACES with the addition of S represents ventral developmental defect [1–3]. Clinical presentation and severity of PHACE syndrome is based on the multi-system involvement of the disorder.

The patients with PHACE syndrome are exposed to different surgical procedures including cerebrovascular, cardiac, and airway surgery. Appropriate preoperative assessment, including a detailed history, physical examination, and investigation are necessary for appropriate perioperative anesthesia care of such cases. Knowledge of the associated anomalies of PHACE syndrome and understanding of the underlying pathophysiology of these anomalies helps anesthesiologists to provide safe and sufficient perioperative management. Major anesthetic concerns and precautions focus mainly on the management of airway hemangiomas, cerebrovascular malformation, and cardiac anomalies.

The presence of airway hemangiomas is the primary concern to anesthesia providers in which, may complicate airway management. Approximately 25% of children with PHACE syndrome have extracutaneous hemangiomas and as many as 52% of them may extend to oropharyngeal airway commonly subglottic hemangiomas [1].

Because of the potential life-threatening airway management, airway evaluation should be considered for PHACE patients with a history of respiratory symptoms, such as unexplained tachypnea, stridor or hoarseness. This may include nasal endoscopy to evaluate the upper airway or more commonly, direct laryngoscopy, and bronchoscopy in the operating room under general anesthesia [1].

Medical therapy may include propranolol, corticosteroids, and vincristine that help to shrink the size of airway hemangiomas. Propranolol therapy is the best choice for infantile hemangiomas (IH) with a reported response rate of 98% [1]. Those medications have a great impact on the perioperative anesthesia care. As hemangiomas may cause significant neurological and cardiovascular morbidity, propranolol therapy controls the growth of hemangiomas and minimizes this risk [6]. A stress dose of hydrocortisone should be considered for patients on prolonged corticosteroid therapy. Hemodynamic effects with potentiation of intraoperative bradycardia, hypotension, or hypoglycemia can result when propranolol is administered on the day of surgery. However, prolonged withdrawal of propranolol therapy may lead to rebound tachycardia and hypertension, which may be harmful to the patient with significant cerebrovascular involvement. Vincristine is a less common therapy for hemangiomas which may result from autonomic or motor neuropathy. Although it has minimal impacts on perioperative anesthetic care, it has been reported to cause isolated vocal cord paresis [7].

On the other hand, surgical interventions may include CO_2 laser ablation, open excision, and tracheostomy for severe airway obstruction under general anesthesia [1].

Prior starting of anesthesia induction, the appropriate airway equipment should be readily available and easily accessible [8]. General anesthesia can be induced safely by the inhalation of sevoflurane in 100% oxygen with the maintenance of spontaneous ventilation. Neuromuscular blocking agents should be avoided. Anticholinergic agents may be helpful to reduce secretions that improve airway visualization and prevent reflex bradycardia that is associated with airway stimulation [1].

In the present case, the patient had airway evaluation at age of 3 months. The patient had facial hemangiomas without signs and symptoms of airway obstruction. However, direct laryngoscopy and bronchoscopy confirmed the presence of hemangiomas in the oropharyngeal and subglottic area. Propranolol therapy was started immediately as it is the best treatment of choice for IH. Hyperkalemia

was developed in the patient and the patient responded well to conservative medical treatment. Hyperkalemia (without electrocardiographic changes) was reported in two children on propranolol therapy for IH. The underlying cause of the hyperkalemia is unknown, but the authors suggested that it was tumor lysis from the large ulcerated IH combined with impaired potassium uptake into cells as the result of β-blockade [9].

The second major anesthetic concern for patients with PHACE syndrome is the presence of arterial malformations that mainly involves the internal carotid artery and its embryonic branches, followed by the middle cerebral artery [10]. Usually, it occurs on the ipsilateral side of the cutaneous hemangiomas and may be present as hypoplasia, tortuosity, stenosis, and occlusion. These anomalies develop in the early embryonic life in less than 5 weeks without clear causes [11].

Clinical severity of these anomaly variables and neurological insults are rare. However, arterial ischemic stroke may occur during childhood and adulthood and may be present as seizures or hemiparesis. Therefore, all patients with PHACE syndrome having a large segmental facial hemangiomas should have appropriate brain imaging to assess and exclude abnormal cerebrovascular structure [5]. Understanding the pathophysiology of cerebrovascular abnormalities is necessary to provide appropriate preoperative anesthesia management. Anesthetic goals, with the presence of these anomalies, focus on maintaining cerebral blood flow (CBF) and oxygen delivery through the smooth and deep level of anesthesia too. All predisposition factors of cerebral ischemia and seizure that may change cerebral perfusion pressure and CBF, especially at induction of anesthesia, should be prevented and managed accordingly if it is present. Neurological consultation should be considered in presence of cerebrovascular involvement for proper neurological assessment and to optimize, document, and administer preoperative anticonvulsant medications.

Cardiovascular anomalies associated with PHACE syndrome are common and may be present in 37% of patients [2]. Coarctation of the aorta and abnormal origin of the subclavian artery are the most common pathology. The other cardiac abnormalities reported include tetralogy of Fallot, septal defects, aortic arch abnormalities, and stenosis of the semilunar valves [5].

Preoperative cardiac consultation and echocardiogram assessment and arterial imaging with MRA should be considered for screening the presence of cardiovascular anomalies. Anesthetic goals focus on maintaining normal heart rate, monitoring blood pressure at proximal and distal to the obstruction to ensure adequate tissues perfusion, and control of the systemic vascular resistance.

Conclusion

PHACE syndrome is a rare disease with serious association of anomalies mainly involving airway, cerebrovascular, and cardiac structure. Appropriate preoperative assessment through history, physical examination, and investigation shows the degree of severity and clinical manifestations of these anomalies. Certain perioperative anesthetic implications should be considered mainly for difficult airway management that related to airway hemangiomas, abnormal cerebrovascular structure, mainly carotid arteries, involvement that affect CBF and results in cerebral ischemia and the association of congenital cardiac disease.

Acknowledgement

None

List of abbreviations

CBF Cerebral blood flow
FOB Fiberoptic bronchoscopy
IH Infantile hemangiomas
MRA Magnetic resonance angiography
PHACE Syndrome Posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe syndrome

Consent for publication

Informed consent was taken from parents to publish this case report in a medical journal.

Ethical approval

Ethical approval is not required at our institution for publishing of a case report in a medical journal.

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Summary of the case

Patient (gender, age)	1	Male, 7 months
Final Diagnosis	2	PHACE syndrome, Hirschsprung disease with colostomy and hyperkalemia
Symptoms	3	Elevated K Level and T wave change in ECG
Medications (generic)	4	Calcium gluconate, salbutamol nebulizer, and sodium bicarbonate, Propranolol
Clinical Procedure	5	Laparoscopic pull-through procedure under general anesthesia
Specialty	6	Pediatric anesthesia and pediatric general surgery