Anesthetic Management of a Pediatric Patient Diagnosed with Bilateral Hereditary Pheochromocytoma: A Case Report*

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ABSTRACT

Pheochromocytoma is a rare, catecholamine secreting tumor, accounting for 1% of pediatric hypertensive patients[1]. In children, pheochromocytoma is even more infrequent and are mostly bilateral[2]. Perioperative management of bilateral pheochromocytoma requires thorough preparation to reduce the consequences of hypotension, hypertension, hypoglycemia, hyperkalemia, and hyponatremia. Mortality of up to 50 % has been reported in the surgical resection of this tumor[2-5]. The challenges of the intraoperative team and how an anxious patient turned cooperative and pleasant shall be discussed.

Keywords: Bilateral Pheochromocytoma, Pediatric Pheochromocytoma.

INTRODUCTION

Pheochromocytoma is a rare but lethal disease in children and accounts for only about 0.1% percent of hypertensive pediatrics. The Philippine Pediatric Society's Pediatric Disease Registry program reported only 7 confirmed cases in the past twenty years according to the ICD code corresponding to Adrenomedullary Hyperfunction, which covers catecholamine secreting Pheochromocytomas.

There are currently no guidelines available to support a particular anesthetic drug or technique.

Randomized clinical trials would not be practical due to its scarcity. More extensive retrospective studies with a sufficient population may be useful in determining the outcomes of different management strategies to make more definitive recommendations. Sustained hypertension, attributed to secretion of norepinephrine, epinephrine, and dopamine were found in more than 60 % of cases. Other symptoms like headaches, excessive sweating, heart palpitations, chest pain, abdominal pain, nausea, vomiting, diarrhea, constipation, pallor, weakness, weight loss seizure, [6] and anxiety may also occur. If left untreated pheochromocytomas may cause serious, life- threatening complications, including cardiomyopathy, myocarditis, cerebral hemorrhage, and pulmonary edema. The only definitive treatment is surgical resection.

However, tumor resection should not be attempted without a comprehensive reoperative medical preparation to maintain volume status and counter all the catecholamine-induced cardiovascular effects that may occur intraoperatively. Thus, anesthetic management of pheochromocytoma is complicated and challenging, especially when both adrenals will be removed. A multidisciplinary team's intensive preoperative preparation, vigilant intraoperative, and comprehensive postoperative care are undeniably essential to provide the safest and optimal care to these patients.

CASE DESCRIPTION:

Our patient is a 12-year-old boy from Bataan, a son of an office worker mother. He weighed 36.5 kilograms with a height of 157cm. Nine months before admission, he had increasing episodes of headaches with no known triggers. He was given Paracetamol 500mg/tab one tablet as needed by his mother. Eight months before admission, the patient suddenly experienced successive seizure episodes described as body rigidity with upward rolling of the eyeballs accompanied by loss of consciousness. He consulted a nearby hospital in Bataan, where they first discovered he has hypertension (BP 220/110mmHg). A Whole abdomen CT scan

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revealed two suprarenal masses on both sides, and his urine metanephrine test was elevated. Patient's mother revealed, she lost her husband due to pheochromocytoma five years ago (age = 35). After all work-ups were completed; he was diagnosed to have pheochromocytoma and was advised to go to Manila for further management.

He was given Metoprolol 50mg/tab one tab BID and Valproic Acid 500mg/tab one tab in AM and ½ tab in the evening, as take-home medications.

He sought consult and was admitted in our institution. He was admitted 1 month prior to the procedure for preoperative blood pressure control, oral Terazosin, 1mg/tab one tab every 12 hours was added to his other medications. The physical exam findings on admission revealed a well-nourished, conscious, coherent, not in cardiorespiratory distress boy. His vital signs were as follows: BP 154/82 mmHg, PR 103 bpm, RR 16-22/ CPM. His neurologic exam was normal. Likewise, all laboratories, including CBC, platelet, and chest x-ray, were normal.

Preoperatively, the patient fasted for more than 6 hours. However, venoclysis began soon as he was placed on NPO with D5NM at 76-77 cc/hr. A proton pump inhibitor was given at midnight. His maintenance medications were given at 5 am with 15 cc water. CBG monitoring done every 4 hours confirmed normoglycemia.

In the Operating Room, the patient had an NIBP, five lead ECG, and pulse oximeter. His initial vitals were: BP 176/94 mmHg, PR 124 bpm, RR of 18-20 CPM, and O2 saturation of 99% on room air. A Lumbar Epidural catheter was inserted on the first attempt, with the patient on his right lateral decubitus, with a Tuohy Gauge 20 needle. Insertion of the arterial line and IJ catheter were done after induction of general inhalational endotracheal anesthesia. Fentanyl and Nicardipine infusions were prepared and placed on standby before endotracheal intubation along with Epinephrine and Norepinephrine drips.

His vital signs before induction were as follows: BP 131/75 mmHg, PR 98 bpm, RR 20 CPM. Temperature: 36.7 C. He was induced with propofol 2.7mg/kg/IV, was administered Rocuronium 0.5 mg/kg, to facilitate endotracheal tube insertion, and maintained with sevoflurane at 3 volume %. His vitals immediately after intubation were:: BP 92/65 to 110/72 mmHg, Heart rate:72 -90 bpm. An endotracheal tube size 7.0 was secured after one attempt using direct laryngoscopy with Macintosh Blade 3.0 at level 19. An arterial line was placed on the left, while the IJ catheter was on the right internal jugular vein. A rectal probe was also inserted for temperature monitoring. At the initial stages of surgery, no elevations in BP and HR were noted.

However, soon as the right adrenal gland was manipulated, the patient's BP rose to 180-200 mmHg SBP. Thus, fentanyl infusion 2-3 mcg/kg/hr and nicardipine (0.5-3 mcg/kg/min) infusions were started. The patient's blood pressure dropped from 130 to 70 to 90 systolic when the right adrenal gland was detached. Therefore, the nicardipine drip was stopped, and the fentanyl drip was titrated. Norepinephrine and epinephrine drip was initiated at 0.02 to 0.20 mcg/kg/hour and titrated. Isolation of the left adrenal gland caused the same elevations of blood pressure, while its removal caused hypotension. The surgeon also disclosed he had inadvertently injured a part of the patient's inferior vena cava, which caused bleeding. Thus, immediately, one unit of prbc was transfused. The rest of the operation was uneventful. The team decided not to extubate the patient immediately, and titrated norepinephrine to maintain SBP to at least 100mmHg. CBG throughout the OR was noted to be within normal limits ranging from 80-112mg/ml.

He was transferred to the Pediatric Intensive Care Unit (PICU), still intubated for closer postoperative care. ABG done read compensated metabolic acidosis with adequate oxygenation. Sodium Bicarbonate was administered. Postoperative pain relief was through a continuous Bupivacaine 0.1% drip via the EC running at 20cc/hr combined with Paracetamol 8mg/kg/IV Q6 and Ketorolac 0.55mg/kg/IV Q6 and Hydrocortisone 10mg/IV. At the third hour of PICU stay, the patient spontaneously opened his eyes while breathing on his own. He was awake, alert, and follows directions. The patient also claimed to have a very mild pain score at 2/10. His vital signs were as

follows: BP 117-72, PR 88, RR 19, Spo2 99% on 5LPM face mask. Hydrocortisone was shifted from 10mg/IV to 6mg/tab every 12 hours. On subsequent visits to the patient, the patient was very cooperative and accommodating towards the team, no longer complains of headaches, and was cheerful and thankful.

DISCUSSION

Patients with pheochromocytoma have excessive stores of catecholamines in the sympathetic nerve terminals, and norepinephrine released from these terminals gets access to receptors on the effector cells readily.[6], Adrenoceptor overstimulation of catecholamines leads to the [7] signs and symptoms of pheochromocytoma. These catecholamine attacks can strike any time, resulting in serious hard to manage emergencies. Therefore, early diagnosis and surgical management are undeniably recommended. Though it is true, surgical removal of PCC is curative in 90% of the cases. However, in order to prevent catecholamine crisis, a comprehensive preoperative evaluation and preoperative preparation by the well- coordinated multidisciplinary team was key to the successful perioperative management of this case[8].

Blood pressure control for a minimum of 3-5 days
Systolic blood pressure value <130 mmHg*
Diastolic blood pressure values <80 mmHg*
Heart rate <80 beats/min
Orthostatic hypotension with blood pressure >80/45 mmHg
Ventricular arrhythmias <1 in 5 min
No ST-T wave changes in ECG
Hematocrit <45

The values may differ according to various institutional protocols and author preferences. *BP of <160/90 mmHg may be acceptable according to few authors. BP:Blood pressure, ECG:Electrocardiography

Table 1: Goals of preoperative alpha blockade [9]

Roizen *et al.* in 1982 proposed a set of criteria (now called the Roizen criteria) to objectively determine the adequacy of preoperative alpha blockade, and they include[10]:

1. No in-hospital blood pressure >160/90 mmHg for 24 h prior to surgery;
2. No orthostatic hypotension with blood pressure <80/45 mmHg;
3. No ST or T wave changes for 1-week prior to surgery;
4. No more than 5 premature Ventricular contractions per minute.

Mortality rates of pheochromocytoma resection was reported to decrease from 45% to 0% if patients were treated with alpha blockade.[10] Therefore, addition of Terazocin to the patient's maintenance meds was very valuable. Terazocin provided the necessary alpha blockade necessary to minimized the potential impact of an unopposed alpha vasoconstriction. Preoperative alpha blockade is crucial to maintain intraoperative hemodynamic stability and minimize morbidity during resection.[10] Phenoxybenzamine, a non-selective alpha adrenergic blocker, is the first line drug used for preoperative blockade, but is unavailable in the Philippines. Recently, Bongon et. al reported that Terazosin, a selective alpha-1 antagonist, at a maximum dose of 4 mg per day, may be safely given to Filipino patients diagnosed with pheochromocytoma for preoperative blockade. He further recommended its use as first line agent in the pre-operative management of pheochromocytoma in the Philippines[11]. From a hemodynamic perspective, few other clinical situations present a more complex and life-threatening situation than Pheochromocytoma resection. In this fragile perioperative environment, the anesthesiologist must be organized, systematic, prepared and well equipped in anticipation of the resections of the adrenal masses.

Relief from anxiety before anesthetic induction is essential, as fretfulness can predispose to catecholamine release. Administration of Midazolam .08mg/kg/IV and Fentanyl 0.5mcg/kg/IV was therefore given before induction to curtail hypertension. All vasopressor pumps were prepared and ready to be administered at any time. The epidural catheter was inserted with ease, and induction was stress-free. Induction was done with propofol because it has been documented as safe in these patients[12] Rocorunium was the muscle relaxant of choice because of its inability to cause histamine release.

Sevoflurane was used to maintain general anesthesia and was found to be the agent of choice forcardiovascular stability in pheochromocytoma.[13]

An arterial line was connected for a more accurate real-time blood pressure and volume status monitoring. An IJ catheter was also inserted to serve as wide bore access for fluid therapy and a port to the central vascular compartment for expeditious infusions of vasodilators and vasoconstrictors. The excellent outcome of this case may have been because of an effective preoperative blockade and an adequately filled volume compartment, having been prepared by the multidisciplinary team of physicians. The only challenge was when the surgeon started handling the tumor, which reoccurred with the second tumor manipulation. However, this was quickly corrected after titrating the vasopressors along with the judicious use of balanced crystalloids. Tumor manipulation usually generates dramatic pressor responses, which is expected because of the increases in levels of norepinephrine and epinephrine during tumor handling.[14] When the surgeon started tumor resection, it was noticeable that the patient had episodes of severe bradycardia, accompanied by episodes of hypertension and tachyarrhythmias, treated immediately by the prepared vasopressors. Blood transfusion was straightaway delivered when bleeding was perceived. Titrating the depth of anesthesia, rapidly administering direct arterial vasodilators, and blood curtailed any catastrophic hemodynamic consequences. It cannot be overstated that the anticipation and preparedness along with the knowledge and understanding of the pathophysiology and pharmacology was able to prevent any complication.

CONCLUSION AND RECOMMENDATIONS:

The anesthetic management of a child with pheochromocytoma poses significant challenges. Knowledge and understanding of pathophysiology and pharmacology are crucial to provide the safest anesthetic care. The comprehensive preparation and well-coordinated teamwork by the multidisciplinary team of doctors provided a suitable perioperative environment that effected a positive outcome. A further look into other anesthetic modalities such as the utility of thoracic epidural anesthesia, total intravenous anesthesia with propofol and remifentanil may prove beneficial in preventing the consequences of catecholamine surges of pheochromocytoma.

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