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Perioperative anesthetic management in pediatric with pheochromocytoma tumor resection

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ABSTRACT

Pheochromocytomas (PCC) is rare neuroendocrine tumors which present as the malignant and familial features. These catecholamine-secreting tumors have classic triad symptoms of headache, sweating, and palpitation primarily due to the release of catecholamines and their metabolites in the body with hypertensive crisis become its predominant clinical symptoms. The excessive release of catecholamines may produce a life-threatening hemodynamic surge during the intraoperative period. Therefore preoperative preparation and intraoperative monitoring become an essential point. Nevertheless, postoperative care is also a critical issue to curtail its morbidity and mortality rates further.

Keywords: pheochromocytoma, catecholamines, hypertensive crisis
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INTRODUCTION

Pheochromocytomas (PCC) is rarely seen among the pediatric population, and its intraoperative management is as similar as an adult case. The majority of patients have refractory hypertension as the most common clinical presentation; hence the comprehensive optimization prior surgery should be mandatory.[1] The careful assessment of several preoperative risk factors and prevention of untoward perioperative complications - induced hemodynamic turmoil to lead to the main favorable physiology and pharmacologic aspects in optimizing perioperative outcome.

CASE REPORT

A 13-year-old, 34 kg male presented with severe headache and history of hypertension recognized since six months prior. His headache has been getting worse and further followed by blurry vision complaints. The previous medical history revealed hemorrhagic stroke without hemiparesis sequelae. He was treated in the intermediate ward to optimize his blood pressure with Captopril 50mg every 8 hours, extended release of nifedipine 30 mg every 24 hours and titrated nicardipine infusion. His blood pressure range was in 170-200/100-120 mmHg.

Complete blood count showed normal leucocyte count (10.52 x 10^3/uL), slightly decreased hemoglobin (10.71 g/dL), normal hematocrit (32.33%), and normal platelet (465.3 x 10^3/uL). His coagulation profile returned normal, as well as his chemical blood panels and electrolytes. The imaging result of plain abdominal x-ray was unremarkable. Meanwhile, further test by abdominal CT angiography showed bilateral benign masses on the suprarenal site suspected PCC or renal without the significant appearance of stenosis, aneurysm, thrombus, or arteriovenous malformation (AVM) in descendent aortic, abdominal aortic, along with both side left and right of renal and iliac communicant arteries. Preoperative echocardiography has only found mild tricuspid regurgitation (TR) with normal left ventricle (LV) systolic function, with acceptable ejection fraction (EF) of 80.73%.

He was scheduled for tumor removal. Upon arrival at the preparation room, his blood pressure (BP) was 150/100 mmHg (mean arterial pressure/MAP was 116 mmHg), tachycardia with heart rate (HR) 130 beat per minute (bpm), and otherwise were unremarkable. He was given premedication intravenously (IV) with midazolam 2 mg IV and fentanyl 15 mcg. The continuous nicardipine infusion was initially set to 3 mcg/kg/hour; then we gradually titrated it to reach a 20% reduction of MAP (to about 93 mmHg).

A standard ASA monitoring along with arterial line monitoring and central venous catheter (CVC) was attached. He received pre-oxygenation and dexmedetomidine loading dose 1 mcg/kg within 10 minutes, continued with 0.2-0.7 mcg/kg/min as maintenance. Induction of anesthesia was given with titrated propofol 70 mg, fentanyl 70 mcg, and rocuronium 40 mg. We used air/oxygen mixture with sevoflurane to maintain anesthesia. The target of systolic blood pressure (SBP) was within 120-130 mmHg and HR 80-100 bpm which were achieved by adjustment and titration doses of dexmedetomidine, nitroglycerin, and nicardipine. The urine production was targeted to 0.5-1 mL/kg/hour and body temperature 36.5-37.5°C.

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During surgery, the removal of the left suprarenal tumor was uneventful. Meanwhile, there was massive bleeding after right suprarenal tumor resection leads to hypovolemic shock. It happened after releasing tumor out of inferior vena cava. The blood pressure immediately dropped to 60/30 mmHg. Hence the fluid resuscitation with massive blood transfusion protocols of the packed red cell (PRC) and fresh frozen plasma (FFP) was promptly administered. The vasodilators drugs were stopped and switched to inotropic and vasoconstrictor with adrenaline, norepinephrine, and dobutamine along with continued ketamine infusion as maintenance.

Furthermore, vasopressin and hydrocortisone were given to overcome the post-resection vasoplegic effect. At the end of the surgery, his hemodynamic state was kept stable with BP range within 110-120/70-90 mmHg, HR 90-100 bpm, SpO2 99% on controlled ventilation, and urine output 0.8 mL/kgBW/hour. We transferred him to the Pediatric Intensive Care Unit (PICU) for intensive monitoring and tapered off the doses of dobutamine, vasopressin, and norepinephrine.

He was brought to fully awake status and extubated on the third day after the surgery, and the hemodynamic state was gradually returning to initial preoperative level (140-170/90-110 mmHg). Hence blood pressure medication was continued by nicardipine infusion only. Proper blood glucose monitoring was also addressed with targeted level to 110-180 mg/dL. He was admitted in PICU for seven days and discharged after 11 days of total admission with last recorded BP was 120/80 mmHg with amlodipine 10 mg every 24 hours as his take-home medicine. Anatomical pathology result was per PCC morphological features.

DISCUSSION

PCC is a rare catecholamine-secreting tumor of suprarenal medulla with its annual incidence rate is around 0.2-0.8 per 100.000 population. The genetic mutation is known as a predominant cause which is an autosomal dominant inherited. The classical eponym of "ten-percentage tumor" from PCC itself is referred to some features namely 10% are malignant, 10% are the extra-adrenal site, 10% are familial, 10% are found bilaterally, and 10% are in normotensive patients. However, these initial attributes may not be longer used due to several recent contradictory studies which have otherwise found that higher tumor proportions with malignant trait as high as 29%, the extra-adrenal site reaches to 24%, and familial origin extends to 32% proportion.[2]

PCC has classic triad symptoms of headache, sweating, and palpitation primarily due to the release of catecholamines and their metabolites in the body. Furthermore, the other constitutional symptoms include hypertension, fatigue, sweating, nausea, weight loss, constipation, feverish and pallor-appearance. Long-standing exposure to the catecholamines accumulation lead to dilated cardiomyopathy, ventricular failure, myocardial infarction, arrhythmia, stroke, and other cardiovascular ischemic diseases.

The clinical symptoms of headache and hypertension are mostly associated with norepinephrine-secreting tumors, meanwhile other symptoms for instance palpitation, sweating, anxious, and panic attack are suspected due to epinephrine or dopamine secreting tumors. Sympathetic nervous system stimulation releases an excessive amount of norepinephrine on the synaptic cleft which will manifest as hypertensive crisis.[3]

The aims of preoperative management include control of arterial pressure, heart rate and arrhythmia, restoring of intravascular volume depletion, myocardial function optimization, as well as improve the blood glucose and electrolyte disturbance. PCC tumor resection belongs to one of the crucial challenges for an anesthesiologist with regards to careful monitoring of hemodynamic stability due to several anaesthesia-induced catecholamine releases procedures, for example during direct laryngoscopy and intubation procedures, peritoneum insufflation, surgery stimulations, and tumor removal, followed by some unpredictable possible complication post ligations. The meticulous perioperative anesthesia planning and not to mention, the thoughtful communication with the surgeon will be needed.

The first key point is how to overcome the patient's anxiety before induction to avoid any upsurges of catecholamine release. Ideally, a long-acting benzodiazepine class, for instance, lorazepam or diazepam should be administered one-night prior surgery along with midazolam intravenously just before the patient is transferred to the operating theatre. It is useful for patient relief and put them on less susceptible state towards induction-induced hypertensive crisis.

It is an absolute indication to administer invasive arterial pressure monitoring in all of the patients with PCC prior anesthesia induction as the continuous beat-to-beat monitoring will bring hemodynamic state through closely observed, especially during direct laryngoscopy and endotracheal intubation. A large bore of peripheral IV should also be placed routinely.[4] Histamine receptor-2 antagonist (H_2 blockers) can be given as an option, however certain antiemetic, for instance, metoclopramide should be avoided as it triggers a sudden hypertensive crisis. Furthermore, short-acting

Alpha 1 antagonists can be given in the morning prior surgery, nevertheless the administration of longer-acting agents, for instance, phenoxybenzamine and doxazosin should be postponed 12-24 hours before surgery.

The most common induction agents of choice are etomidate and propofol. The airway instrumentation procedure should be done only after the patient have been reached an appropriate depth of anesthesia to prevent sudden tachycardia and hypertensive crisis. The use of all the drugs which may precipitate histamine release must be averted, and neuromuscular blocker agent usage just before laryngoscopy becomes crucial. The most favorable agent of choice is vecuronium it has no any either autonomic effect or histamine release, and it is frequently used as paralytic agents of PCC resection. Pressor effect attenuation due to direct laryngoscopy becomes the main aspect over anesthesia induction, and common additional drugs should be given include a small dose of fentanyl, intravenous lidocaine, esmolol 0.5 mg/kg bolus and continued infusion as indicated, along with nitroglycerin, nicardipine, and sodium nitroprusside as indicated. Inhalation agents, for instance, enflurane and sevoflurane are routinely used in the past as a result of their less-fluctuating hemodynamic profile and non - arrhythmogenic effect. Nitrous oxide can also be used.[5]

The opiate use varies on the approach, patient tolerance, and hemodynamic issues. Long-acting opiates agents, for example, morphine and hydromorphone are widely used, although several later studies have successfully reported the use of remifentanil as well. In the past few years, spinal and epidural regional technique anesthesia have been preferably used with satisfying results. Nevertheless, the caution should be warranted regarding hemodynamic response.[1] Hypertension might be provoked by several surgery stimulations for instance positioning, incision, and intubation procedure; however, it tends to be temporary and responds rapidly to the therapy.

On the other hand, tumor manipulation may precipitate much more dramatic effects in response to an increase of epinephrine and norepinephrine level in plasma. The hemodynamic crisis is typically mediated by epinephrine or norepinephrine (it depends on the predominant type of catecholamine released by a tumor) and manifested as extreme bradycardia followed by hypertension or severe tachycardia and tachyarrhythmia. The prompt management includes deepening the depth of anesthesia and immediate arterial vasodilator administration, which sodium nitroprusside becomes mainstay therapy about nitroglycerin to reduce preload. These both medications have a rapid onset of action and easily titrated. In refractory cases, nicardipine and fenoldopam have been used successfully. The furthest dopamine (DA-1) agonist causes peripheral vasodilatation with increasing renal blood flow concomitantly. Magnesium sulfate has also been used widely for hemodynamic control regarding its strong vasodilator effect which acts as direct catecholamine receptor inhibition in PCC resection. It also exhibits a strong calcium antagonist effect. The comprehensive communication with the surgeon is a crucial aspect prior manipulation of that tumor in diminishing sudden hemodynamic instability. Since hyperglycemic fluctuation often occurs due to an excessive catecholamine amount and insulin infusion therapy, hence it also has to be routinely managed.

The abrupt changes of hypotension might be caused by tumor ligation in relation with contracted plasma volume, surgical bleeding, and anesthesia-induced vasodilation which provoke profound and refractory hypotension. To a certain extent, an essential communication with the surgeon will possible to restore this deteriorating state by administering a large volume of bolus infusion just before that ligation procedure. The use of a vasoactive agent, DA-1, norepinephrine, and vasopressin are also beneficial, especially in a refractory circulatory shock which the acute vasopressin therapy has been increasingly preferred. It is due to the nondependent effect of vasopressin to the peripheral adrenergic receptor for its pressor effect after tumor resection. Several recent findings have documented the use of IV methylene blue, particularly for hemodynamic rescue after resection. It may act through a cyclic guanosine monophosphate inhibition mechanism which responsible in vasoplegic syndromes. The steroid administration might also be considered for a patient undergoing bilateral adrenalectomies with persistent hypotensive.[6]

Postoperative care has to be delivered in the intensive care unit, and invasive blood pressure monitoring should be conducted in the first 24 hours. Postoperative hypertension might be provoked by unbearable pain, previous history of essential hypertension, urinary retention, and fluid overload. Furthermore, incomplete tumor removal or even metastatic process may cause postoperative persistent hypertension. Long term steroid therapy is indicated for a patient who underwent bilateral adrenalectomies surgery. Appropriate monitoring of blood glucose is also important as the postoperative rebound hypoglycemia may occur in relation with no longer existence of norepinephrine inhibitory effect towards insulin-secreting cells; furthermore, this symptom might also be masked by β-*blocker* administration.[7]

CONCLUSION

PCC tumor represents significant challenges for anesthetist with regards to optimizing its perioperative management approach and reducing morbidity and mortality rate which are related to its resection procedure. The meticulous understanding of its pathophysiology and pharmacological agents used before surgery, along with intensive hemodynamic monitoring will eventually determine the successful outcome of the surgical intervention.

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