



Anesthesia management for pheochromocytoma removal in a 17-year-old girl: Case report

17 yaşında kız hastada feokromasitoma eksizyonu için uygulanan anestezi yönetimi: Olgu sunumu

Gülşen Keskin,¹ Mine Akın,¹ Sibel Saydam,¹ Sengül Özmert,¹ Yeşim Şenaylı,¹ Feyza Sever,¹ Devrim Tanıl Kurt,¹ Emrah Şenel²

¹Department of Anesthesiology, University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, Ankara, Turkey

²Department of Pediatric Surgery, Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey

Abstract

A rare tumor of the chromaffin tissue, pheochromocytoma is characterized by increased secretion of catecholamines. Pediatric cases represent only 5% of all pheochromocytomas. In this report, we presented anesthesia management of a 17-year-old girl who would undergo right suprarenal mass excision due to pheochromocytoma accompanied with familial Mediterranean fever (FMF). Preoperative blood pressure control was achieved with phenoxybenzamine. General anesthesia was established with thiopental, vecuronium, fentanyl, and sevoflurane. Sodium nitroprusside and phentolamine was used for perioperative blood pressure control. Tramadol and diclofenac were administered for postoperative pain. The patient was discharged after a good preoperative preparation and perioperative management with uneventful treatment period.

Keywords: Anesthesia; child; familial mediterranean fever; pheochromocytoma.

Despite being rarely seen in childhood, pheochromocytoma is regarded as the most common endocrine tumor. It is usually seen during adolescence and manifests itself as hypertension.^[1] Pheochromocytomas are mostly benign and surgical resection provides curative treatment. However, catecholamine release during the surgery or absence of catecholamines after removal of the mass may lead to sudden hemodynamic alterations, increasing perioperative mortality.^[2]

FMF is an autosomal recessive-linked genetic disorder, which

Özet

Kromafin dokularının nadir bir tümörü olan feokromasitoma yüksek miktarda katekolamin salgılanmasıyla karakterizedir. Bu tümörlerin sadece %5'i çocuk popülasyonunda tanımlanmıştır. Bu makalede feokromasitomanın yanında ailesel Akdeniz ateşi (FMF) de bulunan 17 yaşındaki kız hastanın sağ sürrenal kitlesinin eksizyonu için uygulanan anestezi yönetimi sunuldu. Hastanın preoperatif kan basıncı kontrolü fenoksibenzamin ile sağlandı. Genel anestezi uygulaması için tiyopental, vekuronyum, fentanil and sevofluran tercih edildi. Peroperatif kan basıncı kontrolünde sodyum nitroprussid ve fentolamin kullanıldı. Postoperatif ağrı kontrolü tramadol ve diklofenak ile sağlandı. Hasta iyi bir preoperatif hazırlık ve peroperatif yönetimle sorunsuz tedavi sürecinin ardından taburcu edildi.

Anahtar Sözcükler: Anestezi; çocuk; ailesel Akdeniz ateşi; feokromasitoma.

is characterized by episodes of recurrent fever, abdominal pain, and serositis. Anesthesia management of FMF patients without complications like amyloidosis does not require special attention, yet anesthesia and surgical stress may trigger FMF attacks.^[3]

In this case report, we discussed our anesthesia management of a pediatric patient with comorbid pheochromocytoma and FMF, where preoperative preparation, intraoperative anesthetic follow-up and management, and postoperative follow-up warranted individualized care.



Case Report

A 17-year-old girl applied to emergency room with complaint of headache. She had sweating, weakness, headache, and joint pain. Past medical history showed diagnosis of FMF for 6 months treated with oral colchicine 0.5 mg twice daily. Family history revealed hypertension in her mother, uncle, and grandmother. In physical examination, her weight was 50 kg, blood pressure (BP) 170/130 mmHg, heart rate (HR) 76 beats per minute (bpm). Laboratory findings showed no abnormality except a plasma noradrenaline level of 2626 mg/ml. Plasma and urine catecholamine values were presented at Table 1.

There was left axis deviation on electrocardiogram (ECG) and hypertrophic interventricular septum on echocardiography. Abdominal magnetic resonance imaging (MRI) showed masses 45x40x30 mm in the right adrenal gland. As oral amlodipine 10 mg daily do not sufficiently control preoperative hypertension, oral phenoxybenzamine 2.5 mg three times daily with concomitant citalopram for 2 weeks was administered. During this period, BP varied 110/60 to 135/80 mmHg in supine position, and HR varied 84 to 117 bpm. Hematocrit was 44.3%, blood glucose was 83 mg/dL, and other laboratory results were within normal range. Two days before the surgery, intravenous (iv) infusion of crystalloid (dextrose 5%, NaCl 0.2% enriched with KCl) 50 ml/kg//24h was initiated. Upon decision of mass excision with laparotomy, the patient was consulted to anesthesia department where she was considered as ASA III. She and her parents also gave written informed consent. Premedication was performed with midazolam 2 mg iv and ranitidine 50 mg iv 30 min. before the surgery. Standard monitoring including ECG, pulse oximetry, non-invasive blood pressure, and end-tidal CO₂ was applied in operating room. Left radial artery cannulation was performed under local anesthesia. Anesthesia was induced with iv 1 mg/kg of lidocaine 2%, 375 mg of pentothal sodium, 0.1 mg/kg of vecuronium bromide, and 2 µg/kg of fentanyl. Maintenance anesthesia was established with sevoflurane 2% in O₂-N₂O mixture and bolus doses of vecuronium bromide were used, if required. After endotracheal intubation, esophageal temperature probe and urinary catheter was inserted. Right jugular vein was catheterized. Blood gases, electrolytes, and glucose were assessed regularly. Postoperative analgesia was provided with 1.5 mg/kg of iv tramadol 1.5 mg/kg and 50 mg of intramuscular diclofenac sodium. When the mass was being touched,

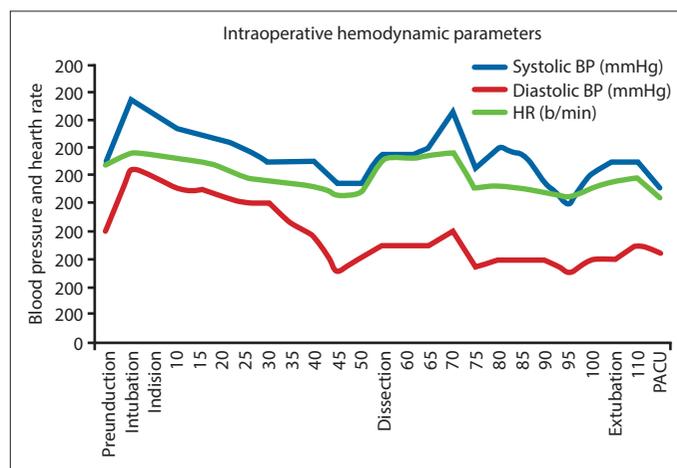


Figure 1. Intraoperative hemodynamic parameters.

the arterial pressure was escalating. We administered sodium nitroglycerin infusion 0.3 µg/kg/min. When arterial blood pressure was not controlled, we started iv bolus doses of phentolamine, which was repeated six times at 2.5 mg dose when arterial blood pressure ranged from 140/100 mmHg to 170/100 mmHg. Intraoperative hemodynamic parameters are demonstrated at Figure 1.

During the surgery, Ringer's lactate was infused at a rate of 10 mg/kg/h. Before the mass was removed, hydroxyethyl starch 6% was administered at 10 ml/kg/h infusion rate. En bloc removal of the mass was performed. After removal, BP was 130/90 mmHg. Total duration of the anesthesia was 135 minutes. A total of 2000 mL fluid was administered with a urinary output of 600 mL. Postoperative hemoglobin was 11.3 g/dL, hematocrit 32.9%, and blood glucose 12.6 mg/dL. Hemodynamic parameters were stable during intensive care stay with no need for antihypertensive medication. Blood glucose, complete blood count, and urinary output were within normal ranges. Pathological examination confirmed the diagnosis of pheochromocytoma. The patient was discharged from the hospital on postoperative day 6.

Discussion

Pheochromocytoma is rare in children, constituting only 5% of all cases. Male to female ratio among children is 2:1. The majority (85-90%) of pheochromocytomas are solitary tumors

Table 1. Preoperative and postoperative catecholamine levels

Parameters	Preoperative level	Postoperative level	Reference range
Plasma			
Noradrenaline (mg/ml)	2626	544	0-400
Adrenaline (mg/ml)	<15	<15	0-85
Urine/24 h			
Vanilylmandelic acid (µL)	3,2	2	0-6
Metanephrine (µL)	10,7	30	0-320

localized to a single, usually the right, adrenal gland. It is the reason for 0.1% of all hypertensive disease. In 10% of cases, familial disease exists.^[4] In our case, a family history of hypertension was present. The mother, uncle, and grandmother of the patient were examined by endocrinology clinic; however, results of their assessment were unknown. There were none of other disease or syndromes.

Main clinical features of pheochromocytoma include paroxysmal headache, hypertension, sweating, and palpitation. In our case, headache was the reason for admission to the hospital where BP was measured as 170/130 mmHg.

The diagnosis was established by measuring 24-hour urinary catecholamines and their metabolites, i.e. metanephrine and vanillylmandelic acid (VMA). 24-hour urinary VMA and metanephrine assessment has a 97% sensitivity and 91% specificity. In our patient, urinary VMA and metanephrine levels were within normal range yet plasma noradrenaline levels were found elevated. Location of the tumor could be detected by MRI or computerized tomography (2). A 45x40x30 mm solid mass of the patient was visualized by MRI with right suprarenal localization.

Since hypersecretion of catecholamines during anesthesia induction, intubation, and surgical tumor resection could elicit hypertensive crisis, adequate adrenergic blockade and volume replacement is very critical for preoperative preparation. Nonselective α -blockers, selective α -blockers, β -blockers, or calcium channel blockers may be used for adrenergic blockade. First choice in children is the phenoxybenzamine, a haloalkylamine which irreversibly inhibits α_1 and α_2 receptors.^[5] Its primary side effects are postural hypotension and reflex tachycardia. Other side effects include headache, dry mouth, and nasal congestion. Phenoxybenzamine also restores volume gap beside hypertension and hyperglycemia. It was also used in our patient at thrice-daily oral dose of 2.5 mg for two weeks preoperative to control hypertension.

Anesthesia management aims to provide adequate depth and cardiovascular stability. It is relatively critical due to hemodynamic fluctuations,^[6] which are, in fact, most common problem in pheochromocytoma patients. Main purpose of preoperative pharmacological treatment is to establish an optimal blood pressure and heart rate.

Since life-threatening BP alterations may occur during induction and manipulation of the tumor, central venous catheterization is required to monitor arterial pressure and ensure any prompt medical interventions if these alterations occur.^[7] We also performed invasive arterial pressure monitoring by left radial artery cannulation before the induction.

During perioperative period, none of anesthetic techniques or drugs have been shown to be superior over others and drugs that causes release of histamines are usually avoided. Induction of anesthesia should be very smooth to avoid changes in hemodynamic parameters. Our case was pre-medicated with midazolam. Thiopental sodium is among acceptable induction agents, and opioids should also be used. Vecuronium is

the most preferred neuromuscular agent due to its minimal influence on cardiovascular system. IV lidocaine and fentanyl should be administered one minute before intubation to reduce sympathetic response to laryngoscopy. For maintaining anesthesia, sevoflurane could be used.

If hypertension is present in deep anesthesia, sodium nitroprusside infusion should be started. If this fails, iv phentolamine should be given in single doses. In our case, phentolamine and sodium nitroprusside were used successfully; there was no need to use β -blocker.

Hypotensive attacks may occur after adrenal vein ligation due to diminished catecholamine plasma concentrations. This condition is tolerated by volume administration and discontinuation of antihypertensive agents. Epinephrine, norepinephrine, phenylephrine, dopamine, or vasopressin infusions are rarely required.^[8]

For resection of adrenal masses below 6 cm and/or 100 g, laparoscopic approaches are preferred in experienced centers.^[9] Nevertheless, pneumoperitoneum and hypercapnia during laparoscopic adrenalectomy may give rise to elevation in catecholamine release, and hence, sudden hemodynamic alterations. In our case with FMF comorbidity, our limited laparoscopic experience led us to prefer open surgery not to cause prolonged surgery time and sudden hemodynamic changes.

We found no case with pheochromocytoma and FMF comorbidity in the literature, which was present in our case. Abdominal crisis occurs in 95% of the patients with FMF.^[10] A crisis may be triggered by stress factors such as anesthesia and surgery.^[11] We believe that no development of an FMF episode during postoperative period could be attributed to the regular use of colchicine and appropriate anesthesia management. Tramadol and diclofenac was sufficient for postoperative analgesia. Patient was closely monitored for hemodynamic parameters, blood glucose, and abdominal crisis. Follow-up showed stable hemodynamics and normal blood glucose levels.

In conclusion, sufficient perioperative preparation, readiness for the problems, and close monitoring could constitute fundamentals for successful anesthetic management of these very occasional cases. This preoperative preparation, anesthesia management, and preference of open surgery could be regarded as successful in this patient with comorbid pheochromocytoma and FMF.

Conflict of interest: There are no relevant conflicts of interest to disclose.

References

1. Pham TH, Moir C, Thompson GB, Zarroug AE, Hamner CE, Farley D, et al. Pheochromocytoma and Paraganglioma in children: A review of medical surgical management at a tertiary care center. *Pediatrics* 2006;118:1109–17.
2. Hack HA. The perioperative management of children with pheochromocytoma. *Paediatr Anaesth* 2000;10 463–76.

3. Weir PS, McLoughlin CC. Anaesthesia for caesarean section in a patient with systemic amyloidosis secondary to familial Mediterranean fever. *Int J Obstet Anesth* 1998;7:271–4.
4. Prabhu M, Joseph TT, Shetty N, Chaudhuri S. Child with bilateral pheochromocytoma and a surgically solitary kidney: Anesthetic challenges. *Saudi J Anaesth* 2013;7:197–9.
5. Ein SH, Pullerits J, Creighton R, Balfe JW. Pediatric pheochromocytoma. A 36 yr review. *Pediatr Surg Int* 1997;12:595–8.
6. Harish R. Pheochromocytoma resection: Current concepts in anesthetic management. *J Anaesthesiol Clin Pharmacol* 2015;31:317–23.
7. Turner MC, Lieberman E, De Quttro V. The perioperative management of pheochromocytoma in children. *Clin Pediatr* 1992;31:583–9.
8. Batra YK, Rajeev S, Menon P, Saxena AK, Rao KL. Anesthetic management of bilateral pheochromocytoma with paradoxical hypotension in a 11-year-old child. *Paediatr Anaesth* 2007;17:295–6.
9. Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al. Pheochromocytoma and paraganglioma: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2014;99:1915–42.
10. Simon A, van der Meer JW, Drenth JP. Familial Mediterranean fever—a not so unusual cause of abdominal pain. *Best Pract Res Clin Gastroenterol* 2005;19:199–213.
11. Oka T, Oka K, Hori T. Mechanisms and mediators of psychological stress-induced rise in core temperature. *Psychosom Med* 2001;63:476–86.