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FULL PAPER

Perioperative anesthetic management in suprarenal pheochromocytoma tumor resection

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Pheochromocytoma is a neuroendocrine tumor that is a malignant degeneration of chromaffin cells in the medulla of the suprarenal gland. Until recently, the mainstay treatment for pheochromocytoma is surgery. A 48 years-old male patient was referred with a diagnosis of left suprarenal tumor. Alpha blockers, specific beta-1 blockers, and calcium channel blockers are recommended for pheochromocytoma. The patient was given doxazosin 1x1mg, amlodipine 1x10 mg and bisoprolol 1x5 mg. Pheochromocytoma surgery can be performed by laparoscopy or by laparotomy. Abdominal CT scan showed a mass in the left suprarenal area with a size of 43 x 54.1 x 46.7 mm and a laparoscopic adrenalectomy was scheduled. Induction agents frequently used are propofol and etomidate. Induction in this case were using fentanyl, propofol, and rocuronium. Maintenance anesthesia used O_2 40%, sevoflurane 1-2 vol%, dexmedetomidine, fentanyl, and rocuronium. After surgery, the patient was admitted in the ICU with relatively stable blood pressure. The patient was given FFP and PRC transfusion due to severe anemia which subsequently showed improvement on the second day. All agents that cause histamine release and sympathetic stimulation should be avoided as much as possible. The recurrence rate for pheochromocytoma is 14% in the primary location or 30% in the extra-adrenal. Therefore, its long-term follow-up is necessary. If there is persistent hypertension for a long period after surgery, suspicion of residual pheochromocytoma tissue should be considered. In this case the blood pressure was 95-110/62-73 mmHg on the first day and 91-113/67-70 mmHg on the second day.

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KEYWORDS

Anesthesia; suprarenal; adrenal; pheochromocytoma; resection.

Introduction

Pheochromocytoma is a rare neuroendocrine tumor, with an incidence of 2-8 cases per million population in the United States. This tumor is a malignant degeneration of chromaffin cells in the medulla of the suprarenal gland which functions to secrete catecholamines, resulting in abnormalities resulting from mass effect and systemic abnormalities related to the body's response to catecholamines. Until now, the main treatment for pheochromocytoma is surgery with many considerations that must be taken into account [1].

Although the incidence is rare, some stages of pheochromocytoma tumors can be life-threatening, with mortality mainly due to

complications of hypertension. Only around 10% to 29% experience malignancy and metastasis. The cause of death in pheochromocytoma patients is complications from excessive catecholamines in the blood, causing unphysiological vascular conditions [2].

The main therapy for pheochromocytoma is surgery to radically remove tumor tissue. There is a problem with removing pheochromocytoma, as there will be a sudden decrease in systemic catecholamines which can cause rapid changes in the patient's vital signs which may lead to death. Therefore, preoperative, intraoperative, and post-operative management is crucial in managing patients with pheochromocytoma. This is supported by the intraoperative mortality rate of 50% due to late diagnosis. However, this can be reduced to 2% in patients who are optimally prepared both pre and post-surgery [3]. Here, we are going to report a 48 years-old male patient who was referred with a diagnosis of left suprarenal tumor and planned laparoscopic adrenalectomy.

Case illustration

A 48-year-old male patient was referred with a diagnosis of left suprarenal tumor and a laparoscopic adrenalectomy was planned. About 6 months earlier, the patient began to frequently complain of headaches, heart palpitations, sweating, feeling hot, calves felt sore and weak, and dizziness when looking down. The average blood pressure is 170-190 mmHg/100-110 mmHg with the highest reaching 220/140 mmHg. The patient then went to Mitra Keluarga Hospital and had a laboratory examination with normal results (Table 1). The patient was prescribed with candesartan 16 mg 1x1, amlodipine 10 mg 1x1 with a mean blood pressure of 140-160/80-100 mmHg. However, the complaints did not improve and were accompanied by recurring abdominal cramps. The patient then underwent abdominal ultrasound and CT scan that revealed a mass in the left suprarenal area, then patient was prescribed with doxasozin 1x1 mg, amlodipine 1x10 mg, and bisoprolol 1x5 mg. In addition, he was advised to undergo tumor removal surgery. There are no food or drug allergies.

Pre-operative evaluation revealed free airway, spontaneous breathing with a rate of 18x/minute, symmetrical, no crackles and wheezing, SpO_2 98% on room air, no ventilation, intubation, supraglottic airway, or cricothyroidotomy difficulty. CRT <2 seconds, warm extremities, pulse 79x/min, blood pressure 127/77 mmHg, regular, normal heart S1 S2, no murmurs and gallops. GCS was 456 and Wong Baker Faces Scale 1-2. Bladder movement is normal. The abdomen is soft and bowel sounds are normal. There is no edema and no fever.

Abdominal CT scan with contrast (Figure 1) showed a solid mass with central necrosis at the left suprarenal gland measuring 43 x 54.1 x 46.7 mm post contrast showing inhomogeneous enhancement and signs of invasiveness. Chest x ray (Figure 2) and Electrocardiography (Figure 3) showed normal results.

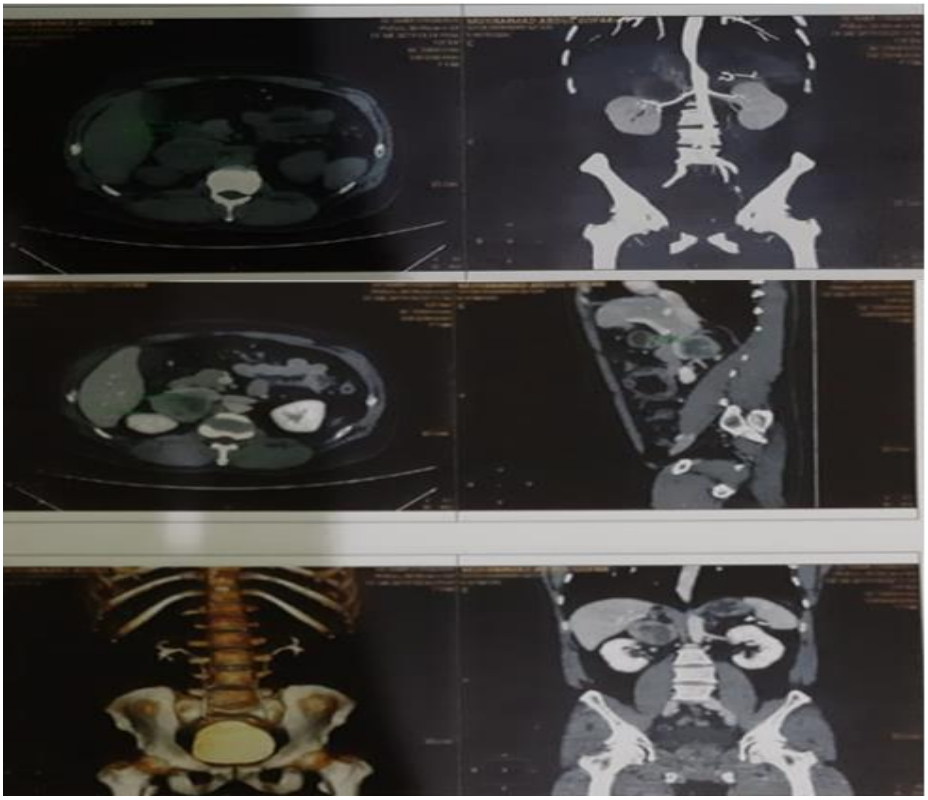

FIGURE 1 Abdominal CT scan with contrast

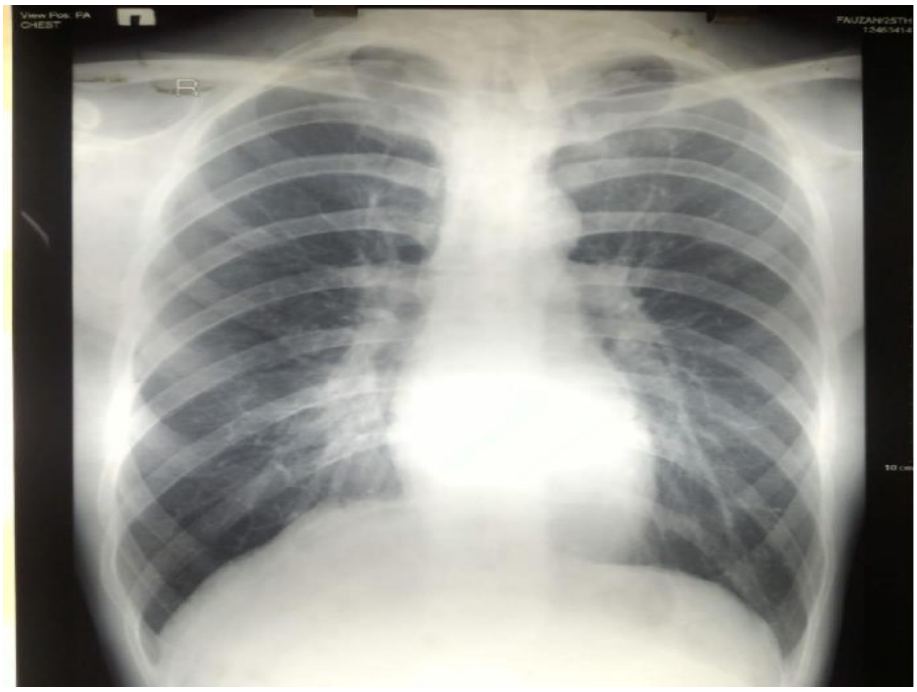

FIGURE 2 Chest X-ray

Intraoperative evaluation showed free airway, RR 20x/minute, SpO_2 98% with room air. On

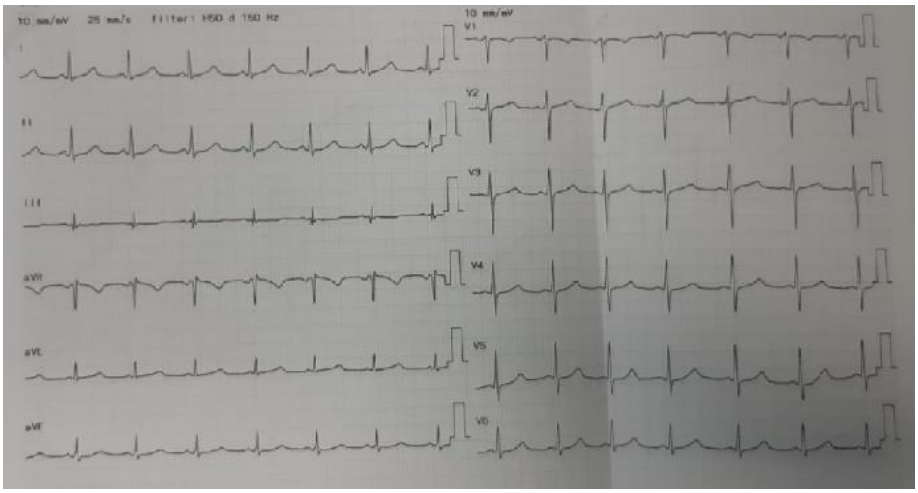

FIGURE 3 Electrocardiography

Lung examination, there were vesicular breath sounds with no crackles or wheezing. Blood pressure was 134/80 mmHg (MAP 100 mmHg), HR 82x/minute, single S1 S2, no gallops or murmurs. ECG showed sinus rhythm, regular, and normoaxis. The patient was then induced with fentanyl 100 mcg, propofol 80 mg + 50 mg, and rocuronium 50 mg with cuffed ETT 7.5 and lip margin 19 cm, right and left breath sounds were symmetrical, and $ETCO_2$ was 39 cm H_2O. Maintenance anesthesia used O_2 40%, Sevoflurane 1-2 vol%, dexmedetomidine 0.4-0.7 mcg/kg/hour, fentanyl 30 mcg/hour, and rocuronium intermittent. Hemodynamics showed a very fluctuative pressure because of excretion of cathecolamine during manipulation, massive bleeding, and shutdown of symphathetic autonomy after adrenal resection. Systolic BP of 60-220 mmHg, a diastolic BP of 35-140 mmHg, and MAP of 42-160 mmHg on arterial blood pressure monitoring. Intraoperative medication includes nicardipine 5-15 mg/jam, NE 100-300 ng/kg/minute, vasopressin 0.02-0,04 IU/minute and metoprolol standby. Fluid balance consisted of urine 500 mL (0.89 mL/kg/hour) and intraoperative bleeding of 3850 mL with RL input of 3000 mL, 1000 mL of colloid, and 1500 mL of whole blood.

On the first post-operative day in the ICU, the patient was sedated. Ventilator was installed with PCV mode, rate 20, PC 20, PEEP 6, I:E 1:2, FiO_2 40%, triggering 2Lpm, TV 360-400, f 20, MV 7, 2-8 lpm, and $ETCO_2$ 36 mmHg. Vesicular breath sounds, no crackles or wheezing bilaterally with SpO_2 96%. PSIMV ventilator mode with PEEP 5, PS 10, Pinsp 17, rate 14, I:E ratio 1:2, trig 2, TV 390 - 414 mL, f total 22-26/minute, MV 8.1-10.3 lpm, $ETCO_2$ 38, and SpO_2 97-99%. The circulatory system showed good perfusion, a warm and dry acral, CRT <2 seconds, HR 87-99 / minute regular, strong pulse, systolic BP 95-110 mmHg, diastolic BP 62-73 mmHg, and MAP 73-86 mmHg on ABP. Abdomen showed post laparotomy wound with negative bowel sounds. The patient was diagnosed with post left nephrectomy, post hemorrhagic shock, and severe anemia. Management consists of ventilator support, slight head up position 30°, personal hygiene 2x/day, RD5 1000mL/24 hours, cefazolin 1gr/8hours, omeprazole 40mg/12hours, paracetamol 1gr/8hours, tranexamic acid 1gr/8hours, midazolam 2 mg/hour, fentanyl 30 mcg/hour, rocuronium 20 mg/hour, NE 50-75 ng/kg/min, epidural ropivacaine 0.18% 5mL/hour, FFP transfusion 813 mL and PRC 215 mL. The condition was demonstrated in Figure 4.

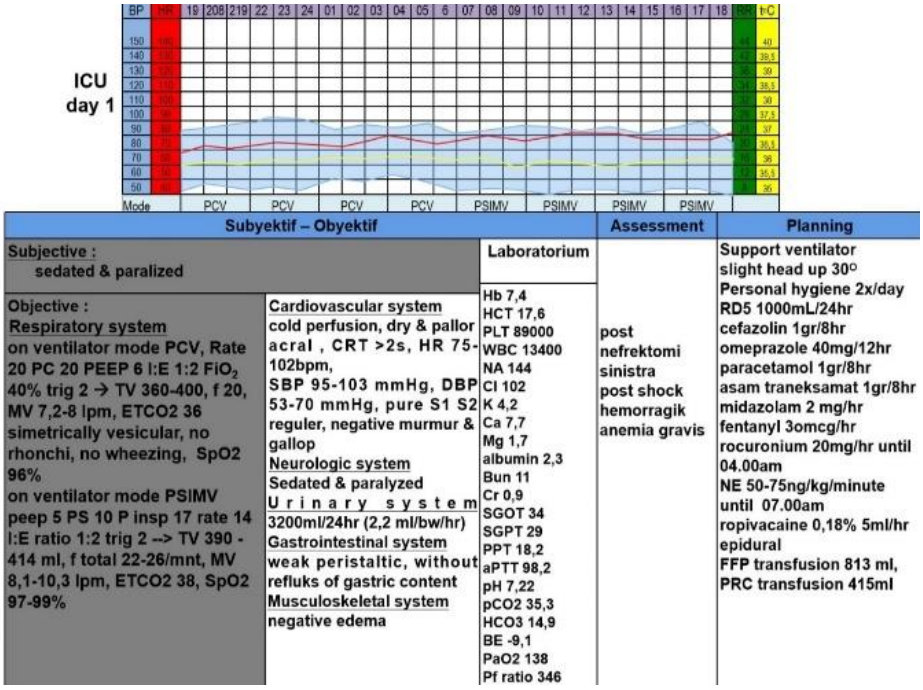

FIGURE 4 Day-1 ICU care

On the second post-operative treatment day, a ventilator was in PSIMV mode, rate 8, PC 14, PS 10, PEEP 4, I:E ratio 1:2, FiO_2 30% trig 2, TV 360-400, f20, MV 7.6 -8.4 lpm, $ETCO_2$ 38, vesicular breath sounds, no crackles or wheezing bilaterally with SpO_2 98%. PSV mode ventilator with PEEP 4, PS 8, FiO_2 30, TV 380 - 420 mL, total f 16-22/minute, MV 7.6-10.1 lpm, $ETCO_2$ 38, SpO_2 99% and T piece installed. Cardiovascular system perfusion warm, dry, red, CRT <2 seconds, HR 70-95 x/minute, systolic blood pressure 91-113 mmHg, diastolic blood pressure 67-70 mmHg, GCS E4MXV6 and after extubation E4M5V6. Abdomen showed post laparotomy wound with positive bowel sounds. Management consists of ventilator support, slight head up position 30°, personal hygiene 2x/day, RD5 500 mL/24 hours, D5 6x100 mL via NGT, cefazolin 1 gr/8 hr, omeprazole 40 mg/12 hr, paracetamol 1 gr/8 hr, tranexamic acid 1 gr/8 hr, metamizole 1 gr/8 hr IV, and PRC transfusion 210 mL. The condition was illustrated in Figure 5.

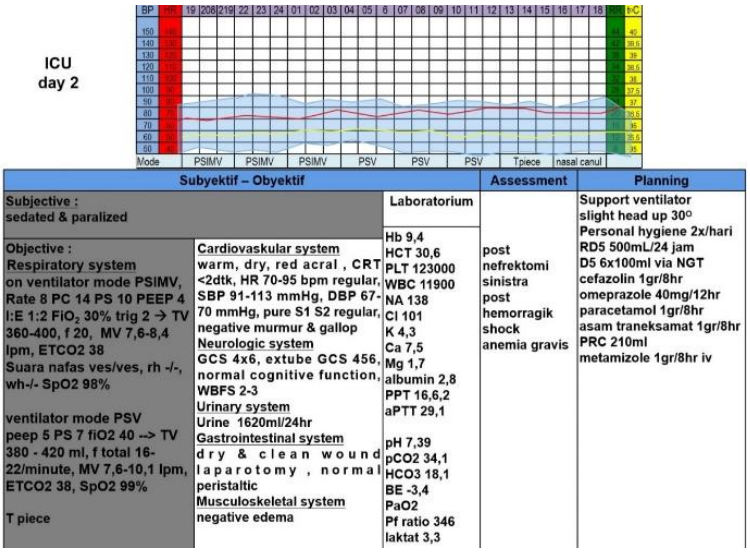

FIGURE 5 Day-2 ICU care

TABLE 1 Laboratory evaluation

Laboratory parameters	Pre-operative	Day 1 post-surgery	Day 2 post-surgery	Day 3 post surgery
Blood				
Hemoglobin	14.5	7.4	9.4	10,1
Hematocrit	41	17,6	30.6	34,2
Leukocytes	9890	13400	11900	9030
Platelets	314000	89000	123000	134000
SGOT	37	34		
SGPT	27	29		
GDA	125	78-133	148	112
Albumin	3,4	2,3	2.8	3.1
PPT	10 (10-14)	20.2	14.6	
APTT	28 (22-30)	98.2	29.1	
BUN	17	11		
Serum creatinine	1.1	0.9		
Na	143	144	138	136
K	4.7	4.2	4.3	4.2
Cl	104	105	101	99
Ca	8.6	7.7	8.1	8.3
Mg		1.7	1.9	
Blood gas analysis				
pH		7.22	7.39	7.38
pCO_2		35.2	34.1	37.3
HCO_3		14.9	18.1	17.8
BE		-9.1	-3.4	-2.9
PaO_2		138	134	91
Pf ratio		346	408	441
Lactate		6.3	4.1	1.9

Discussion

Pheochromocytoma or sympathetic paraganglioma is a tumor that originates from chromaffin cells in the medulla of the adrenal glands. Chromaffin cells secrete catecholamines. Most (90%) pheochromocytomas are unilateral. In bilateral cases, the possibility of genetic abnormalities needs to be considered [4]. However, genetic testing is not effective because it does not change therapy planning and does not determine the prognosis of the disease [5].

Pheochromocytoma is a rare disease, with an incidence of 2-8 million people every year in America. Male and female gender predilection is equal. About 10% of cases are found in children with a high probability of genetic disorders. Pheochromocytoma can be malignant or benign. In benign cases, death is caused by persistent stimulation of adrenergic receptors, causing complications such as in chronic hypertension patients [2]. A 48 years-old male patient was referred from with a diagnosis of left suprarenal tumor, pheochromocytoma suspected.

The adrenal glands are composed of cortex and medulla. In the cortex, there are three zones, namely glomerulosa, fasciculata, and reticularis, from the outermost layer. Glomerulosa zone produces aldosterone [6]. Fasciculata zone converts steroids into cortisol which is then secreted into the

vasculature throughout the body. Reticularis zone plays a role in the formation of androgens [7]. The medulla of the adrenal glands contains chromaffin cells which produce catecholamine hormones, especially epinephrine and norepinephrine (NE). Abnormal growth of chromaffin cells causes pheochromocytoma [8,9].

The catecholamines produced by pheochromocytoma tumors are mostly epinephrine and NE with rapid and robust effects. NE acts on α-1-adrenergic receptors in vascular smooth muscle, causing vasoconstriction and increasing systemic vascular resistance (SVR), resulting in an increase in blood pressure. NE also acts on α-2-adrenergic receptors causing vasoconstriction of coronary blood vessels and vasodilation of peripheral blood vessels. The effect of NE on β-1-adrenergic receptors is positive inotropic which then increases cardiac output and increases blood pressure. In addition, β-1-adrenergic has the function of secreting renin in juxtaglomerular cells. Renin works through sodium restriction and increases blood vessel vasoconstriction, increasing preload and SVR which can increase blood pressure [4].

Catecholamines increase insulin resistance, leading to increased insulin production and decreased glucose uptake. This occurs because catecholamines have an antagonistic effect on glucose utilization through beta-adrenoceptor desensitization, increasing lipolysis, and pro-inflammation which triggers insulin resistance in the liver. There are also cases of hypoglycemia in pheochromocytoma patients after removal of the adrenal glands [10].

Clinical symptoms in 90% of pheochromocytoma patients are hypertension to hypertensive crisis [4]. Features of headache, sweating and palpitations is called classical triad. If left untreated, it can cause cardiomyopathy, heart failure, myocardial infarction, arrhythmia, or stroke [5]. About 6 months earlier, the patient began to frequently complain of headaches, heart palpitations, sweating, feeling hot, calves felt sore and weak, and dizziness when looking down. The average blood pressure is 170-190 mmHg/100-110 mmHg with the highest blood pressure reaching 220/140 mmHg.

Pheochromocytoma multisystem crisis (PMC) is characterized by a tetrad consisting of coma, encephalopathy, hyperthermia, and multi-organ failure. In contrast to a hypertensive crisis, there is hemodynamic instability in PMC, both hypertension and hypotension, and is often referred to as a pheochromocytoma crisis [4].

The mechanism of hypotensive shock after a hypertensive crisis is thought to occur when the heart and vasculature respond to very high amounts of catecholamines, resulting in severe vasoconstriction and hypertensive cardiomyopathy with manifestations such as hypotension. There is also a theory that hypotension occurs due to desensitization of adrenergic receptors which is also found in post-operative pheochromocytoma patients [11].

Pheochromocytoma evaluation is performed by detecting related hormones in plasma or urine. However, this is difficult because catecholamines are highly dependent on stress, activity, intake, and medication. For urine test, urine must be stored for 24 hours as blood NE and epinephrine fluctuate according to the circadian cycle and their half-time in the blood is very short [2]. In this case, the patient had been diagnosed at a previous hospital so it was not explained further in the case.

More advanced techniques use metabolites of NE and epinephrine that is converted by Catechol-O-methyltransferase (COMT). Consensus stated that this is more sensitive than plasma examination and more specific than urine examination [2].

After a positive biochemical examination, imaging examination was performed to assess the location and size of the tumor, including abdominal CT-scan and MRI. Both are

sensitive; however, MRI is superior for delineating soft tissue because the structure of the adrenal glands is surrounded by fatty tissue. Functional imaging can reveal metastases with scintigraphy. This is carried out for patients with suspected metastases, such as those aged >40 years, no previous family history, negative genetic test result, and previous imaging examination found a small pheochromocytoma that produces metanephrine. This examination may also search for extra adrenal pheochromocytoma [2]. Our patient underwent abdominal CT scan with contrast, showing a solid mass with central necrosis at the left suprarenal gland measuring 43x54.1x46.7 mm showed inhomogeneous enhancement and signs of invasiveness.

Another functional examination is a Positron Emission Tomography (PET) scan. It works similar to scintigraphy. The advantage of PET scan over scintigraphy is that it does not mark normal adrenal tissue, thus only pheochromocytoma is visible. Therefore, PET scans have better sensitivity [12].

The principles of surgical removal of adrenal glands are: (1) Radical resection of the tumor, (2) Minimum manipulation of the tumor, (3) Controlling the vascular supply, (4) Sufficient exposure so that surrounding organs are not damaged, (5) If there are genetic factors, bilateral adrenal removal was considered. Diagnostic laparoscopy is performed before definitive surgery to exclude local invasion, evaluate the subcostal port, size, and location of the tumor. In addition, ligation of the adrenal veins can be performed simultaneously [13].

Pheochromocytoma surgery can be performed by laparoscopy or laparotomy. Both have the similar level of safety however laparoscopy may shorten the recovery time compared to laparotomy. Laparotomy is often used in large tumor or if there is an ectopic tumor beyond adrenal gland [2]. In case of our patient, he underwent laparoscopic adrenalectomy converted laparotomy during operation because of massive bleeding and extensive adhering of tumor.

Left-sided pheochromocytoma cases are technically more difficult. The splenic flexure and colon are initially set aside to reach the splenorenal ligament. Medial rotation of the overlying structures is performed to obtain clear exposure of the adrenal glands and veins. Then the Gerota fascia is incised to gain access to the adrenal vein and adrenal glands. Once the adrenal gland is exposed, identify the edges of the gland and separate it from the retroperitoneum, using the periadrenal fat as a handle to comb the posterior portion of the gland. Clamping is carried out with an endovascular stepper to clamp the larger vein and then the specimen can be removed. An increase in CO_2 causes an increase in catecholamine levels, this can be caused initially by direct compression of the tumor, or because changes in perfusion to the tumor organ are reduced. Sometimes hypercapnia and acidosis are stimuli for catecholamine release and hypertension [13].

Important variables to evaluate in preparation for surgery in pheochromocytoma patients are blood pressure, rhythm control, myocardial function, and addressing glucose and electrolyte disturbances. An ECG is needed to assess whether there is hypertrophy, arrhythmia, or a history of myocardial infarction. Systolic and diastolic function also needs to be assessed with echocardiography considering that cardiomyopathy is one of the pheochromocytoma complications [2].
Preoperative evaluation showed blood pressure 127/77 mmHg, regular, S1 S2 normal heart, no murmurs and gallops. ECG showed sinus rhythm, regular, and normoaxis.

As previously explained, hyperglycemia in pheochromocytoma occurs due to an increase in catecholamines in the blood which are responded to by adrenergic receptors to increase blood sugar. Potential electrolyte disturbances in pheochromocytoma are hypokalemia, hypomagnesemia, and

hypocalcemia. Hypocalcemia occurs as plasma catecholamines stimulate beta-2 receptors which increase the activity of the Na/K ATPase pump so that extracellular potassium is reduced and causes hypokalemia. Complications that can occur due to hypokalemia are arrhythmia. Hypokalemia is associated with decreased reabsorption of magnesium in the kidneys, resulting in hypomagnesemia. A complication of hypomagnesemia is respiratory depression. In addition, an increase in urinary calcium secretion was found, resulting in hypocalcemia [14]. Initial electrolyte examination did not show any hypokalemia, hypomagnesemia, or hypocalcemia. In this case, the patient had a normal fasting blood glucose and blood electrolyte.

An important thing to pay attention to in pre-operative preparation is the patient's vital signs which reflects the increased blood catecholamines level. When there are high levels of catecholamines in the plasma but the clinical manifestations are within normal limits, intraoperative monitoring is sufficient to maintain vital signs, otherwise emergency drugs are given if the patient experiences symptoms of pheochromocytoma intraoperatively [15]. Preoperative vital signs were stable with blood pressure of 127/77 mmHg, pulse 79x/minute, spontaneous breathing 18x/minute, SpO_2 98% room air, and CRT <2 seconds.

With the goal of maintaining hemodynamics when facing a surge in catecholamines due to surgical procedures (laryngoscopy, peritoneal insufflation, surgical stimulation, and touching the tumor) followed by a decrease in catecholamines that occurs after ligation of the tumor. Careful preparation and monitoring are needed to prevent patient mortality.

Since 1982, Roizen et al. has proposed preoperative criteria which are targets that must be achieved by the patient and anesthetist before the patient undergoes surgery, namely (1) No blood pressure >160/90 mmHg 24 hours before surgery, (2) No orthostatic hypotension with blood pressure <80/ 45 mmHg, (3) No changes in ST or T waves 1 week before surgery, and (4) No more than 5 premature ventricular contractions in 1 minute [1]. These four preoperative criteria were not met in the case.

Alpha blockers are given 10-14 days before surgery, which aims to reduce the patient's blood pressure by inhibiting catecholamines from carrying out vasoconstriction while also functioning to increase the intravascular volume that is drained out due to the vasoconstriction process. The success of alpha blockers is characterized by normalization of blood pressure accompanied by a slight orthosis in the patient. The alpha blocker that is often used is phenoxybenzamine, especially during a hypertensive crisis. The dose can be started from 2x10 mg IV as the initial dose, followed by 1 mg/kg or 2x10 mg orally, which then increased every 48 hours according to the blood pressure target indicated by the presence of postural hypotension. Other agents are prazosin and terazosin at a dose of 2-5 mg 2-3 times a day which can be increased to a maximum of 32 mg/day [1]. The successful alpha blockade is reflected by normalizing blood pressure with mild orthostasis. The beta blockade should never be initiated before the alpha blockade. They should be started only after an adequate length of the alpha blockade is established; if not, a hypertensive crisis can occur due to unopposed alpha-receptor stimulation [16]. In this case, the patient was given an alpha blocker with doxasozin at a dose of 1x1 mg.

Calcium channel blockers (CCB) inhibit the calcium influx caused by norepinephrine and have been used to control hemodynamics before surgery. If alpha blockers have been given, CCB functions as adjuvant therapy and is not recommended as monotherapy unless the patient only suffers from mild hypertension or orthostatic hypotension occurs after giving alpha blockers. Nicardipine sustained-release 2x30 mg is often preferred

by anesthetists as additional therapy [2]. In this case the patient was given CCB with amlodipine 1x10 mg.

The recommended treatment for pheochromocytoma includes a high sodium diet and fluid intake to restore blood volume before surgery. This approach aims to reverse catecholamine-induced blood volume contraction. Preoperative intravenous rehydration has been found to be ineffective in optimizing perioperative hemodynamics or improving early outcomes as per some authors. However, restoring blood volume before surgery can reduce the risk of protracted hypotension or shock resulting from sudden vasodilation during surgery, according to some authors. The absence of preoperative volume expansion can be an effective predictor of HI involvement, and guidelines recommend liberal preoperative volume administration [17].

Tachyarrhythmias can occur in pheochromocytoma patients due to catecholamines from the tumor or due to side effects of alpha blockers. Selective beta-1 antagonists are administered after completion of alpha blocker therapy. Selective beta-1 was chosen because beta-2 has a vasodilation effect which can exacerbate vasoconstriction. Administration of beta-1 blockers prevents the rebound vasodilatory effects of alpha blockers [2]. Beta blockers should not be given before alpha blockers. This can aggravate vasoconstriction and can lead to hypertensive crisis. Apart from that, a body that is accustomed to high blood pressure will compensate by increasing the secretion of catecholamines centrally and peripherally [1]. In this case the patient is given beta-1 selective antagonist with bisoprolol at a dose of 1x5 mg.

Managing anxiety before anesthesia is important, because anxiety predisposes to catecholamine spikes during induction. Ideally, the use of long-acting benzodiazepines such as lorazepam and diazepam given the night before surgery, or by administering IV midazolam can calm the patient and reduce the possibility of a hypertensive crisis during induction. Otherwise, this patient was not given any anxiolytic drug because he looked very calm without any sign and symptom of anxiety. Intra-arterial blood pressure monitoring is mandatory for all pheochromocytoma patients who will undergo surgery for blood pressure monitoring because of the possibility of very rapid hemodynamic changes, especially during laryngoscopy and intubation. H_2 blockers are further indicated in patients as needed, especially in cases of anti-emetics. Avoid giving metoclopramide as much as possible as it may precipitate a hypertensive crisis [1].

Frequently used agents for induction are propofol and etomidate. Ketamine should be avoided related to its sympathomimetic properties, similar to ephedrine and meperidine. Airway clearance is performed when sedation is deep enough to prevent tachycardia and hypertension. Propofol has been proven safe, while etomidate has advantages in the hemodynamic stability of patients, especially in patients with hypovolemia [1]. The patient in this case was induced with fentanyl 100 mcg, propofol 80 mg + 50 mg, and rocuronium 50 mg.

All agents that cause histamine release should be avoided as much as possible, this is important in the choice of neuromuscular block agent. Depolarizing muscle relaxants, such as succinylcholine, have the potential to cause a surge of catecholamines originating from muscle fasciculation that can cause mechanical compression of the tumor. Not all non-depolarizing types can be given, for example, pancuronium has a vagolytic effect which can stimulate the release of cathecolamine by symphatetic dominance. So the use of vecuronium is generally used and recommended because it does not cause the release of histamine. Low-dose fentanyl, IV lidocaine, esmolol 0.5 mg/kg bolus, and nitroglycerin, nicardipine, or nitroprusside

infusion can also be given to manage the patient's blood pressure. In recent years, the anesthetic agents used have been enflurane and isoflurane because they have been proven to be safe and do not cause complications in patients. Halothane is contraindicated in pheochromocytoma due to its arrhythmogenic effect by increasing the sensitivity of myocardium to catecholamines. Desflurane has a sympathetic stimulation effect and is not recommended for pheochromocytoma. Sevoflurane is also commonly used for pheochromocytoma patients because it produces a stable hemodynamic profile, is less irritating to the airway than desflurane and has less arrhythmogenic effects [1].

Dexmedetomidine, a highly selective α2-adrenoceptor agonist, specifically targets central receptors and provides sedation, analgesia, and centrally mediated sympatholytic effects. α2 adrenoceptor mediates negative feedback regulation of norepinephrine release at the synaptic terminal in various neuronal cells containing norepinephrine, including adrenal medulla chromaffin cells. Surgical manipulation of adrenal pheochromocytoma causes a substantial release of catecholamines during operation. But during adrenalectomy for pheochromocytoma, where a significant catecholamine release is anticipated, a low dose of dexmedetomidine may be insufficient to adequately suppress catecholamine secretion. Although administration of dexmedetomidine did not directly affect the regulation of catecholamine secretion, it provided hemodynamic stability by reducing maximal blood pressure. Dexmedetomidine served as an effective adjunct to general anesthesia in patients with pheochromocytoma. Intraoperative dexmedetomidine infusion at a dose of 0.5 μg/kg/h in patients undergoing laparoscopic adrenalectomy for pheochromocytoma demonstrated effective mitigation of the increase in maximum BP and HR [18]. Maintenance anesthesia in this patient was using O_2 40%, Sevoflurane 1-2 vol%, dexmedetomidine 0.4-0.7 mcg/kg/hour, and fentanyl 30 mcg/hour, and rocuronium intermitten.

One thing that differentiates surgery to remove pheochromocytoma is the process of managing intraoperative hypertension. Medications used to manage hypertension are phentolamine, nitroprusside, nicardipine, or clevidipine. Phentolamine blocks alpha-adrenergic receptors and blocks the effects of high levels of catecholamines in plasma. Nitroprusside has a fast-acting effect but has a short duration, and acts as a nitric oxide donor as a vasodilator if giving calcium channel blockers alone is not effective. Meanwhile, nicardipine and clevidipine are agents that are often used to control durante blood pressure [19]. Intraoperative medication in our case includes nicardipine 5-15 mg/hour, NE 100-300 ng/kg/minute, vasopressin 0.02-0.04 IU/minute, and metoprolol standby.

Several risk factors that can predict intraoperative hemodynamic instability are high norepinephrine levels before induction, large tumor, falls due to postural hypotension when administering alpha blockers, and MAP> 100 mmHg before induction [2]. In our patient, NE examination was not performed. No other risk factors were found.

Drugs that may increase catecholamines are desflurane, ketamine, morphine, pethidine, atracurium, pancuronium, ephedrine, droperidol, metoclopramide, cocaine, and succinylcholine. Thus, they should be avoided in our patient. Tumor manipulation has the greatest effect in causing catecholamine release. In addition, the release of catecholamines in the blood can increase with pain even without touching the tumor. Increased intra-abdominal pressure can increase catecholamines due to their tumor suppressive effect. This is the consideration for administering capnoperitoneum [2]. In our patient, laparoscopy followed by laparotomy

during operation because of extent adhesive of tumor and massive bleeding intraoperative.

Periods of hypotension are common during surgery, and can occur due to the administration of anesthetic drugs or due to hypertension therapy. Most often hypotension occurs after tumor devascularization, which is generally accompanied by catecholamine resistance. This complication can be overcome with a combination of rapid fluid bolus administration, titration of vasodilators, and administration of alpha agonists [2].

The possible mechanism of hypotension is residual alpha blocker or catecholamine deficiency after tumor removal accompanied by down-regulation of adrenergic receptors due to a chronic increase in previous catecholamines. When discovered, immediately stop the vasodilator agent and administer fluid therapy to the patient. If this method is failed, using NE or vasopressin to increase vascular resistance can be considered [2]. In this case, hypotensive episode due to sudden decrease of cathecolamine following devascularization, denervation, and removal of tumor, exacerbated by massive bleeding of vena renalis laceration during operation.

The condition of hypovolemic/hemorrhagic shock must be addressed immediately to prevent further damage. In patients with hypovolemic shock due to trauma (laceration vena renalis), there is oxygen delivery decreased, due to the decline of stroke volume/cardiac output (drop preload) and decreased Hb. Initially, this condition could be compensated for by increasing the other components from oxygen delivery (raise heart rate, vasoconstriction, and intravascular fluid shift), but if the process of hypo-volemia continues, there will be a condition of greater damage. The target of the given fluid resuscitation is to prevent tissue hypo-perfusion, avoiding “trias of death” (coagulopathy, hypothermia, and acidosis) and avoid organ failure. Shock causes anaerobic metabolism and causes decreased contractions myocard as well as hypothermia. Hypothermia causes coagulopathy, which causes more bleeding and causes the shock to get worse. Cause coagulopathy from bleeding shock caused by tissue damage, fibrinolysis, shock, hypothermia, hemodilution, acidosis, inflammation, and hypocalcemia. Shock causes anaerobic metabolism and causes decreased contraction of myocard as well as hypothermia. Hypothermia causes coagulopathy, which causes more bleeding and causes the shock to get worse. Coagulopathy in shock is caused by tissue damage, fibrinolysis, shock, hypothermia, hemodilution, acidosis, inflammation, and hypocalcemia. Apart from restoring the lost blood volume, it is important to stop bleeding as soon as possible. To stop or at least reduce bleeding can be done by damage control resuscitationin a way: damage control surgery (surgery/angiography), permissive hypotension, and hemostatic resuscitation. [20]. In this patient, unfortunately damage control surgery must be done by left nephrectomy because of massive fragile extent of tumor and massive bleeding from tumor and vena laceration, tranexamic acid, permissive hypotension and replacement of blood loss by crystalloid and colloid.

In case of intraoperative hypertensive crisis, immediate action that should be done, are as follows:

1. Deepening the sedation level,
2. Giving arterial vasodilators, nitroprusside, and/or nitroglycerin, as both are fast in reducing preload
3. Nicardipine and/or fenoldopam, cause peripheral vasodilation.
4. Given a fast-acting beta-blocker infusion to control heart function
5. Magnesium sulfate, which has a vasodilator effect, inhibits the release of catecholamines, and is competitive with calcium [1].

American Society of Anesthesiologists (ASA) stated that intra-arterial monitoring is the gold standard in pheochromocytoma surgery for monitoring blood pressure. Central venous catheters can assess pressure in the right atrium and can also be used to administer large amounts of medication quickly. A Swan-Ganz catheter is able to assess cardiac output, venous oxygen saturation and pulmonary capillary pressure [21]. This catheter is recommended for patients at high risk of heart failure due to cardiomyopathy and pulmonary hypertension. This catheter can be used post-operatively to regulate fluid balance [1,22,23].

All pheochromocytoma patients must receive intensive care after tumor resection, especially monitoring intra-arterial blood pressure to monitor hemodynamics. If after surgery the patient experiences hemodynamic instability, then sedation and installation of a ventilator are necessary because catecholamine production is related to pain, emotions, and patient activity. In our case, arterial blood pressure monitoring was installed before induction.

Open laparotomy may require epidural pain control. Extreme caution must be utilized in epidural dosing as hemodynamic changes can occur rapidly during surgery. Frequently the epidural is placed preoperatively and not utilized until hemodynamic stability with the tumor removed is achieved. Laparoscopic and particularly single-incision retroperitoneal support rarely requires epidural pain management. Pain can be controlled using IV and PO pain medication [24]. In our case, pain is managed by fentanyl and epidural ropivacaine.

Postoperative electrolyte balance must always be evaluated, especially potassium which can decrease further due to reactivation of insulin. Then monitoring blood glucose levels is necessary because insulin activation again causes glucose to be mobilized intracellularly. This transfer of glucose makes the cells hypertonic, thus mobilizing fluid towards the intracellular, giving the impression of a lack of vascular fluid accompanied by vasodilation that has not yet recovered, so that fluid therapy and administration of vasoconstrictive agents are needed if necessary [1]. Post-operatively, the patient in the case was treated in the ICU with a ventilator installed. Electrolyte balance and blood glucose remain evaluated. In this patient, random blood sugar was slight low (78 mg/dL) on the first hours of day-1 and became normal on the next evaluation (138, 148, and 112 mg/dL). The electrolyte was normal. Post-operative management on the first day consisted of a slight head up the position of 30°, paracetamol 1 gr/8 hours, tranexamic acid 1 gr/8 hours, midazolam 2 mg/hour, fentanyl 30 mcg/hour, rocuronium 20 mg/hour, NE 50-75 ng/kg/min, epidural ropivacaine 0.18% 5 mL/hour, FFP transfusion 813 mL and PRC 415 mL because the patient experienced severe anemia after hemorrhagic shock.

Substitution of the function of the adrenal cortex, namely mineralocorticoids, and glucocorticoids, with long-term steroids is necessary for patients undergoing bilateral adrenal gland resection. The commonly used regimen is, hydrocortisone 100 mg given every 8 hours before surgery. In the first 72 hours after surgery, the hydrocortisone dose was reduced to 2x25 mg/day, then changed to oral prednisolone [2]. If after surgery for pheochromocytoma there is persistent hypertension for a long time, it is necessary to suspect that there may still be pheochromocytoma tissue. The recurrence rate for pheochromocytoma is 14% in the primary location or 30% in the extra-adrenal location. So it is necessary to carry out long-term follow-up on patients [1]. In this case there was no persistent hypertension with blood pressure of 95-110/62-73 mmHg on the first post-operative day and 91-113/67-70 mmHg on the second post-operative day.

Conclusion

A 48 years-old male patient was referred with a diagnosis of left suprarenal tumor. Abdominal CT scan showed a mass in the left suprarenal area measuring 43x54.1x46.7 mm and a laparoscopic adrenalectomy was planned. The patient was induced with fentanyl, propofol, and rocuronium. After surgery, the patient was treated in the ICU with relatively stable blood pressure, namely 95-110/62-73 mmHg on the first day and 91-113/67-70 mmHg on the second day.

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Conflict of Interest

There is no conflict of interest.

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