Abstract: A 24yr male presented with complaints of abdominal pain, palpitations, and paroxysms of sweating, headache for past 4 months. He was diagnosed as a case of extra-adrenal pheochromocytoma and started on prazosin, amlodipine, and propranolol. The patient was taken up for surgery after adequate preoperative optimization. Anesthesia was given with proper care and precaution. Intra operative period was uneventful except for a hypotension after tumor vein ligation. Patient became hemodynamically stable after adequate volume replacement and inotropes. He was extubated and sent to high dependency unit for hemodynamic monitoring.

Keyword: Pheochromocytoma, Anesthetic management, Alpha adrenergic blocker, Extraadrenal

INTRODUCTION:
Pheochromocytoma is a catecholamine secreting tumor that arise from chromaffin cells of the sympathoadrenal system. They account for <0.1% of all cases of hypertension in adults. Although they are a rare cause of hypertension, their detection is essential since they have a lethal potential and are one of the curable forms of hypertension. They present a great challenge to the anesthesiologist both in the operating room and in ICU due to their high morbidity and mortality rates. The periods of greatest danger occur secondary to hypertension and arrhythmias during anesthetic induction, intubation, skin incision, abdominal exploration and during tumor manipulation. Preoperative optimization is the most important factor in reducing morbidity and mortality.

CASE REPORT: A 24 year old male patient presented with complaints of abdominal pain, palpitations, paroxysms of sweating and headache for the past four months. On examination his blood pressure was 178/110 mm Hg. He was investigated for the cause and diagnosed as pheochromocytoma. His Vanillymandelic acid (VMA) 24-hr urine collection concentration was 80 mcmol/day (normal 5-25 mcmol/day) and plasma free Normetanephrine was 430pg/ml. MRI of the abdomen showed well defined
large rounded mass seen in the left paravertebral area measuring around 4 × 6 cm displacing the left kidney downward. The suprarenal glands and liver are found to be normal. Echocardiogram showed mild globular LV systolic dysfunction. He was started on Tab. Prazosin 1mg TDS and Tab. Amlodipine 5mg BD for the past one week. Three days after starting the antihypertensive medications, the blood pressure was controlled and the readings were in the range of 124/70 to 142/80 mmHg. He was scheduled to undergo open tumor resection.

Patient was referred to Anesthesia Department for assessment. He had no history of other comorbid illness and no history of previous surgery. His effort tolerance was 6 METS. On examination he was conscious, comfortable, and afebrile. He was not anemic, and there was no cyanosis, no clubbing, no icterus, and no generalized lymphadenopathy. The examination of cardiovascular, respiratory, central nervous systems and abdomen showed no obvious abnormality. Investigations showed, Hb% -9.3gms%, PCV: 32.3, TC: 13,000 cells/cu.mm, Blood sugar -98 mg/dl, Blood urea -27mg/dl, Sr.creatinine-1mg/dl, Na⁺ - 138mEq, K⁺ - 3.8mEq,Blood group - O+ve, platelets – 400000/ cu mm, urine- albumin & sugar- negative. Chest x-ray showed no abnormality, USG abdomen revealed a left paravertebral mass, CT & MRI abdomen diagnosed a 4x6 cm size left paravertebral mass, ECG showed left ventricular hypertrophy. Airway examination showed MMS II, IID >5cms, TMD >6cms, Neck movement was normal and he had no loose tooth. His weight was 64 kgs. His pulse rate was 96 per minute and supine blood pressure was 146/90. His standing blood pressure was measured which revealed no postural hypotension. The plan was to increase the oral dose of prazosin gradually till start of full alpha adrenergic blockade with postural hypotension. Intravenous fluid hydration regimen was started with 1500 ml/day normal saline 0.9%.Five days later, he was reassessed and no postural hypotension was recorded. The dose of Prazosin was again increased to 2mg thrice daily with continuation of I.V hydration. Two days later he developed postural hypotension; supine blood pressure in a range of 114-128/64-78 mmHg and standing blood pressure in a range of 86-90/50-60 mmHg. ECG showed sinus tachycardia with a heart rate of 115 beats/min with no evidence of PVCs. Tab propranolol 40 mg BD was started to reduce the pulse rate to 80-90 Bpm. The hematocrit dropped from 32 prior to 27 following intravenous hydration therapy. Patient was assessed and fit for surgery under ASA III/ MMS II. Premedication was achieved with oral diazepam 5 mg night before. The anti hypertensives were continued as scheduled with no interruption.

He was planned to be taken up under general anesthesia with epidural analgesia. On the day of surgery in the operation room he was connected to non-invasive monitoring: five ECG leads, pulse oximeter, non-invasive blood pressure monitoring and EtCo2 monitor. The following were readily available to use in case of emergency, 1. Nitroglycerine infusion 2. Propofol infusion 3. Esmolol infusion 4.Dopamine infusion 5. Noradrenaline infusion 6.lidocaine 7.Phenylephrine.8. Defibrillator. Two18G intravenous cannulae one in left and other in the right upper limb were secured. Under strict aseptic precautions and under local anesthesia right internal jugular vein cannulated with 7Fr triple lumen catheter. Under strict aseptic precautions 18G epidural needle was introduced at T10- T11 interspace, catheter tip was kept at T8. Three ml of 1.5% lignocaine with adrenaline was given.
as test dose to rule out subarachnoid or intravascular tip placement.
Inj. Glycopyrrolate 0.2mg and inj. Fentanyl 150 mic gm iv was given as premedication. Pre oxygenation with 100% O2 was done for 5 minutes. Induction of anesthesia was started with propofol 120 mg. Bag and mask ventilation was done for 3 minutes. Inj. Xylocard 100 mg was given 90 seconds prior to intubation. Tracheal intubation was facilitated by inj. vecuronium 6mg iv. At induction of anesthesia the blood pressure was 115/82 mmHg and at tracheal intubation it was 105/70 mmHg. Intubation was done with 8 size cuffed endotracheal tube/ Cormack lehane score I. Anesthesia was maintained with N2O: O2 - 2:1 and Isoflurane 0.8 – 1%. After commencement of GA, bladder was catheterized and nasogastric tube was inserted.

Intra operative increase in blood pressure was managed with titrated infusion of nitroglycerine, infusion of Propofol, Esmolol bolus, and increasing concentration of isoflurane. After the tumor vein ligation nitroglycerine, propofol, and esmolol were stopped to avoid hypotension. During surgery central venous pressure (CVP) was maintained around 12-14 cm H2O with fluid infusion at a rate of 10-15 ml/kg/hr of colloids and crystalloids. Inspite of that patient developed moderate hypotension after tumor vein ligation which was successfully managed with i.v fluids, i.v phenylephrine 150 mcg in two doses and dopamine infusion. Otherwise intraoperative period was uneventful. The blood sugar was maintained between 150 – 200 mg during the intraoperative period.

The duration of surgery was 3 hours. Fluids infused during the surgery were crystalloids 3000ml, colloid (Hetastarch) 500ml, whole blood 500ml. The total blood loss during the procedure was 600ml. Urine output was 1100ml. Patient was reversed with neostigmine 3mg and Glycopyrrolate 400 mcg gm. After thorough oral suctioning and adequate neuromuscular recovery patient was extubated. After extubation, patient was conscious, oriented, responded to commands. His BP was 102/70 mm Hg and PR was 106/ minute. Patient was sent to PACU for hemodynamic monitoring and two days later he was discharged to regular surgical ward. Histopathology of the specimen confirmed the diagnosis of pheochromocytoma.

**DISCUSSION:**
Failure of involution of chromaffin tissues in childhood is the cause for extra adrenal pheochromocytoma. Most pheochromocytomas secrete norepinephrine either alone or more commonly combined with a smaller amount of epinephrine in a ratio of 85:15. The normal adrenal gland secretes epinephrine in larger amount. (Ratio is 85:15). In predominantly norepinephrine secreting tumor the systolic and diastolic blood pressure is increased and associated with relative bradycardia. In predominantly epinephrine secreting tumors (15%), the systolic blood pressure is increased, the diastolic blood pressure is decreased and associated with tachycardia.

These neuroendocrine tumors secrete heterogeneous patterns of catecholamines and their metabolites; consequently, the simultaneous measurement of more than one analyte had been the traditional recommendation until recently. Current studies show that plasma free metanephrine levels are the biochemical test of choice for excluding pheochromocytoma. Since the 24-hour urinary total metanephrines and catecholamines have a specificity up to 99% and yield fewer false-positive results, urine studies are a suitable alternative for ruling out pheochromocytoma. Drugs, diet, and stressors can result in elevated plasma catecholamines, which can confound diagnostic studies. Acetaminophen can interfere with plasma
metanephrine assays; therefore, it should not be administered 5 days prior to biochemical testing. Other medications that may affect laboratory assays include tricyclic antidepressants and antipsychotics, levodopa, ethanol, and withdrawal from clonidine. Caffeinated beverages contain the catechol caffeic acid, which interferes with assays of plasma catecholamines and metanephrines. Nicotine can also affect results because it raises plasma catecholamine levels. Finally, standing and emotional stress stimulate the release of catecholamines. To minimize these sources of false positive catecholamine elevation, interfering medications should be stopped at least 2 weeks prior and blood samples should be drawn in the supine position after an overnight fast.

CT can detect adrenal pheochromocytomas with a sensitivity of 99%.(10) Magnetic resonance imaging (MRI) also has excellent sensitivity, approaching 100%; however, the sensitivities for both CT and MRI decrease to below 91% when the tumor is extra-adrenal.(3) Scintigraphy with metaiodobenzylguanidine (MIBG) is often employed to visualize extra-adrenal and recurrent tumors not detected by conventional measures. Although 131 I MIBG has a specificity of greater than 95%, it is not routinely used to diagnose pheochromocytoma because it only has a sensitivity of 77%. 123 I MIBG improves sensitivity to almost 90% because it is particularly useful in detecting tumors with fibrosis or tumors in unusual locations or areas with distorted anatomy.(14)

Pre-operative optimization of patients with pheochromocytoma is an essential part in management.(8,24) An \(-\)adrenergic blocker must be given prior to administering a \(-\)adrenergic blocker to avoid unopposed action, which can lead to hypertensive crisis.(3) In our case, we have used high dose alpha-adrenergic blockade prior to beta blocker in the preoperative period and our target was the development of postural hypotension in order to ensure full blockade.

Roizen et al (19) recommended the following preoperative conditions prior to surgery for pheochromocytoma:

(a) Blood pressure < 160/90 mmHg for 24 hr before surgery,

(b) Postural hypotension > 80-45 mmHg,

(c) ECG should be free of any ST-T changes for a week and

(d) No PVCs more than 1 in five min.

In our case we strictly adhered to Roizen’s criteria.

Preoperative alpha-adrenergic blockade is usually achieved by using phenoxybenzamine, but in our case we have used prazosin which has more advantages. Prazosin does not produce reflex tachycardia, has shorter half-life, so dosage can be adjusted rapidly, such that preoperative and postoperative hypotension are less.(1)

ANESTHETIC CONSIDERATIONS:
It is most appropriate to administer an anxiolytic sedative preferably a benzodiazepine as a premedicant to decrease the catecholamine release. Opioids such as morphine which cause histamine release and can induce catecholamine release are undesirable. Atropine is best avoided as it causes tachycardia and even severe hypertension. In our case we have used diazepam, fentanyl and glycopyrrollate.

Regional anesthesia in combination with general anesthesia has been used. Preoperative insertion of epidural catheter runs the risk of hypertension but can be placed with a good sedation and incremental doses of fentanyl 25 – 50 mcg. Prys – Roberts (17) has suggested a rational technique of mid to low thoracic epidural T9 – T10 combined with adequate general anesthesia and selective adrenergic blockers to control the hemodynamic surges.
in response to tumour manipulations. To achieve adequate intraoperative and postoperative analgesia with the epidural, infusion of bupivacaine 0.1-0.125% with fentanyl 2 mcg/ml at the rate of 6-12 ml/hour, is administered after an initial bolus of 8-10 ml of 0.25% bupivacaine in divided doses. (18) The depth of anesthesia is generally more important than the specific agent used because it can inhibit the adrenergic and cardiovascular responses. Avoid drugs or maneuvers that may provoke catecholamine release or exacerbate the catecholamine actions. Morphine and atracurium can cause histamine release which may provoke release of catecholamines from the tumour. Atropine, pancuronium, and succinylcholine are examples of vagolytic drugs that may stimulate the SNS. Metoclopramide and ephedrine have all created significant hypertensive responses. The manipulation of the tumour causes a significant haemodynamic response and both systolic and diastolic blood pressures increase briskly. Sodium nitroprusside (SNP), phentolamine, nitroglycerine and various other agents like magnesium sulphate, nicardipine, diltiazem, esmolol have been used to control intraoperative rises in blood pressure. Sodium nitroprusside is preferred for this purpose. It is a potent arterio-venodilator with a rapid and brief action and is used as a titratable intravenous infusion0.5 mcg/kg/min. Intravenous nitroglycerine (NTG) can also be employed for this purpose. It is a rapid acting agent that mainly affects capacitance vessels. Similar to SNP, its onset and duration are rapid. We have used nitroglycerine infusion in our case. For intraoperative tachycardia and hypertension beta blockers like atenolol, labetalol have been used. Esmolol is the drug of choice because of its rapid action and short duration of action, is easily titrated to control the rate and blood pressure (25). We have used esmolol in our case.

Hypotension following tumour vein ligation is usually significant and occurs secondary to a combination of factors including an immediate decrease in plasma catecholamines, vasodilatation from residual alpha blockade with phenoxybenzamine, sudden increase in venous capacitance, intraoperative fluid and blood loss. Hypotension can be prevented by volume expansion with a colloid, should be done prior to tumour vein ligation. Management of hypotension by fluid replacement is believed to be a factor for lowering operative mortality (4). Vasopressors are ineffective in hypovolemic state (16). If vasopressors have to be used, norepinephrine and phenylephrine are preferred (20). We have used both fluids and phenylephrine during hypotension with immediate favorable response.

With a decrease in plasma catecholamines immediately following resection, insulin levels increase and hypoglycemia may occur (22). This should be corrected with dextrose containing solutions immediately after tumor vein ligation. Patients required monitoring in HDU for the first 24 to 48 hrs in the postoperative period because cardiovascular and metabolic instability can occur. Volume status should be monitored using central venous pressure monitoring. Urine output and level of consciousness should also be monitored. Three most important postoperative complications are hypotension, hypoglycemia and hypertension. Hypotension which is due to the prolonged action of antihypertensive agents (9). Dopamine and Noradrenaline may be required to maintain blood pressure. Hypoglycemia can occur postoperatively and should be monitored for and corrected with dextrose containing solutions.
Hypertension may be due to pain or because of persistent high levels of catecholamines which may take a few days to become normal\(^6\). Adequate pain relief with epidural opioids and parenteral analgesics should be given.

**CONCLUSION:**
The anaesthetic management of patients with pheochromocytoma remains a challenge to even the most experienced of anaesthesiologist, although the perioperative mortality has reduced remarkably. Preoperative control of hypertension with alpha adrenergic blocking agents followed by beta adrenergic blocking drugs and adequate volume expansion is important for reducing the morbidity and mortality. Patients with pheochromocytoma should ideally be managed by an experienced team of endocrinologist, endocrine surgeon and anaesthesiologists. Early involvement of anaesthesiologist in the management of pheochromocytoma patient is the cornerstone for better outcome. In this case report we confirmed that adherence to Roizen’s criteria can lead to successful perioperative management.

**REFERENCE:**


