

# Pheochromocytoma an Adrenaline Addict - A Case Report

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## ABSTRACT

Pheochromocytomas are rare catecholamine secreting neuroendocrine tumours arising from chromaffin cells of the sympathetic nervous system in the adrenal medulla or extra-adrenal paraganglia.

A 20-years-old female presented with paroxysms of abdominal pain, palpitation, sweating and headache since last 2 years. Pheochromocytoma was confirmed by 24 hour urinary catecholamine level and CT of abdomen. After three weeks of preparation, tumour was excised. The following discussion outlines current approaches to preoperative, intraoperative and postoperative anaesthetic management of patients suffering from pheochromocytoma.

**Key words:** Pheochromocytoma, Catecholamines, NE (Norepinephrine) and EPI (Epinephrine)

## CASE REPORT

A 20-years-old female patient presented for pre-operative evaluation for excision of left sided adrenal tumour. She complained of intermittent abdominal pain, excessive sweating, episodic headache since 2 years and palpitations since 6 months. The patient was diagnosed with hypertension two years back and was started on Tabs. Prazosin 15 mg twice daily, Clonidine 100 mg thrice daily, Furosemide 40 mg daily. The patient's previous medical and surgical history was uneventful.

On examination, height was 165 cms and weight 53 kgs. The ASA physical status classification was ASA 3. Mallampatti classification-1. The heart rate was regular, 140 per minute. Her blood pressure in supine position was - 200/130 mm of Hg and standing- 190/120 mm of Hg. Pulse rate was 140 bpm, regular in nature. Rest of the examination was unremarkable [Table/Fig-1-4].

Ophthalmology, Endocrinology and Cardiology opinions were taken. Increase in drug dosage, addition of  $\beta$ -blocker and Calcium Channel blocker was advised.

By second visit, she was receiving tablets Clonidine 100 mg thrice daily, Prazosin 15 mg twice daily, Furosemide 40 mg once daily, Atenolol 50 mg twice daily, Nicardipine 20 mg twice daily and Alprazolam 0.5 mg once daily. Her B.P. was -150/110 mm of Hg in sitting and 150/100 mm of Hg in supine position with a pulse rate of 120 bpm.

Patient was started on Tab. Lorazepam 3 days before surgery for anxiolysis. I.V fluid therapy with 1.5 litres of crystalloid/day was started 3 days prior to ensure hydration. All drugs were continued till day of surgery. Preoperative B.P. in supine position was 120/98 mm of Hg, standing 80/40 mm of Hg with a pulse rate of 88 bpm.

Patient was planned for combined General and epidural Anaesthesia.

Two 18 G I.V. line secured. Two Ringer Lactate started. ECG, SpO<sub>2</sub>, NIBP, CVP and EtCO<sub>2</sub> monitors were arranged. Epidural catheter was secured at T10-T11 level, a test dose of lignocaine 3 cc tried and a bolus of 0.5% bupivacaine 6 cc administered.

Premedication was achieved with I.V. Glycopyrrolate 0.2 mg, Midazolam 2 mg, Fentanyl 100  $\mu$ g, Ondansetron 4 mg and Hydrocortisone 100 mg. Induction of anaesthesia was started

with 100 mg I.V. Lignocaine, Esmolol 5 mg, Inj Propofol 120 mg and tracheal intubation was facilitated by Vecuronium 4 mg I.V. At induction of anaesthesia BP was 110/80 mm of Hg and post intubation it was 100/70 mm of Hg.

CVP triple lumen 18G line was secured under asepsis. Blood pressure was monitored. Continuous ECG, PR, and EtCO<sub>2</sub> monitoring was done. CVP and urine output were measured every half an hour. Patient was started on I.V. Vecuronium infusion of 3 mg/hr-1, epidural infusion of 0.125% bupivacaine with fentanyl 25  $\mu$ g at 6ml/ hr and maintained throughout the duration of surgery. SNP infusion started at 0.5  $\mu$ g/kgmin-1 at incision and titrated according to B.P. with maximum dose at 1  $\mu$ g/kgmin-1. Propofol infusion started at 100mg/hr-1. Inj fentanyl 50  $\mu$ g I.V. was repeated at 1.5 hr and 3 hrs. CVP was maintained around 10cms of H<sub>2</sub>O.

Intraoperatively, vitals remained stable. After ligation of main adrenal vein, patient's B.P. and P.R. increased. Administered Esmolol bolus 5 mg which was repeated after 15 min, Esmolol infusion 50  $\mu$ g/kgmin-1 was started and tapered accordingly. Multiple draining veins were ligated. B.P. reduced, Esmolol infusion and SNP infusion were stopped.

Patient received 10 crystalloids and 2 colloids over 4 hrs and sustained a blood loss of 400 ml. Urine output was 2500 ml over 4 hrs. Post-operatively patient was not on any vasodilators/vasopressors. Patient was reversed with inj. Glycopyrrolate 0.4 mg and Neostigmine 2.5 mg after adequate respiratory efforts. Patient was not extubated, as she was drowsy and was shifted to ICU with 'T' piece, O<sub>2</sub> support and was continuously monitored. Post-operative vitals- B.P.-120/90 mm of Hg, P.R.-88 bpm, SpO<sub>2</sub> on room air was 100% [Table/Fig-5].

The same evening, patient was extubated as she was conscious and was monitored in ICU for 2 post operative days. On second post-operative day patient had increase in B.P. -150/100 mm Hg, Tab clonidine 100 mg once daily was resumed and was planned to withdraw gradually. Patient was receiving epidural analgesia postoperatively. Glucose level monitoring was done every second hour. Patient was shifted out of ICU on 3rd post-operative day.

Follow up on 3rd week revealed reduction in urine catecholamine levels. Patient was tapered off from Clonidine. Histopathology confirmed "Pheochromocytoma".

Hb - 12 g%
ESR - 10 mm 1st hour
RBS - 88mg/dl
Blood Urea- 30mg/dl, Serum Creatinine- 0.6 mg/dl
Serum Electrolytes- Sodium-137 mmol/L, Potassium-4.6 mmol/L, Calcium- 9 mg/dl
ECG-Tachycardia, LVH with strain pattern.
Thyroid function tests-within normal limits
PT-15.4 S INR-1.16

[Table/Fig-1]: Investigation reports

Renal Doppler- within normal limits
CT whole body-head and neck-Normal, chest-Normal, abdomen: adrenal-heterogenous left adrenal mass 4.6x3.6x5.2mm, no evidence of extra adrenal Pheochromocytoma.
2D Echo- left ventricular hypertrophy with mild TR with 58% ejection fraction.
Chest X Ray- normal lungs fields with cardiomegaly.
MIBG-revealed no extra adrenal involvement

[Table/Fig-2]: Imaging studies



[Table/Fig-3]: CT showing left-sided adrenal mass

Urine VMA- 164.4 mmol/ 24 hrs.
Cortisol- 248.4 mmol/ L
Epinephrine- 98.9 µg/ 24hrs
Noradrenaline- 4794.84 µg/ 24hrs
Dopamine- 2536.98 µg/ 24hrs

[Table/Fig-4]: Urine biochemistry



[Table/Fig-5]: Intraoperative specimen of tumour

To assess adequacy of preoperative management of Pheochromocytoma, following Roizen criteria should be met:
No in-hospital B.P. >160/90 mm Hg for 24 hours prior to surgery.
No orthostatic hypotension with B.P. <80/45 mm Hg.
No ST or T wave changes for 1 week prior to surgery.
Not more than 5 premature ventricular contractions per minute <sup>11</sup> .

[Table/Fig-6]: Roizen criteria

## DISCUSSION

The World Health Organization defines pheochromocytoma as a tumour from catecholamine-producing chromaffin cells in adrenal medulla—an intra-adrenal paraganglioma [7,8]. Usually, found in adrenal medulla but they may arise anywhere in the body [7].

Patient's symptoms reflect excessive secretion of catecholamines into circulation [9]. Clinical presentation varies from triad of episodic headache, diaphoresis and palpitations to a variety of non-specific symptomatology. Most frequent symptom of Pheochromocytoma is hypertension.

Prolonged exposure of the circulation to high norepinephrine concentration results in constriction, of both arteriolar and venous circulation, with a decrease in circulating volume [1,10].

The best confirmatory test is to measure free catecholamines and their metabolites in a 24 hrs urine collection [11,1].

MRI and CT both provide accurate and consistent identification of Pheochromocytomas [12]. Tumours in unusual sites and metastases may have to be identified with metaiodobenzguinidine (MIBG) scintigraphy [10].

A clinical evaluation of the cardiac status of the patient is to be done. A baseline and serial monitoring of full blood count and haematocrit provides an assessment of the adequacy of volume expansion when  $\alpha$ -blockade has been started [13].

### Preoperative investigations

Blood glucose level measurement is needed as hyperglycaemia is common.

**ECG:** ST and T changes secondary to myocardial ischemia, ventricular hypertrophy, arrhythmias.

Chest X-ray may reveal cardiomegaly or pulmonary oedema [1].

**2D ECHO:** to estimate myocardial function if cardiomyopathy is suspected.

Renal function can be assessed using Urea, Creatinine and electrolytes.

Prior to surgery, it is necessary to control arterial pressure, heart rate and arrhythmias and to restore the blood volume to normal [14,13]. This is conventionally done with  $\alpha$ -blockade over a period of 10-14 days and subsequently, additional  $\beta$ -blockade is required to treat any tachyarrhythmias [1].

Prazosin (2-5 mg twice or thrice a day), selective  $\alpha$ 1-blocker, is favoured because of its shorter half life and ease of titration to the desired end point.

$\beta$ -blockade is not instituted until  $\alpha$ -blockade is established. A non selective  $\beta$  blocker should not be instituted before  $\alpha$  blockade is achieved as blockade of  $\beta$  2 vasodilatory receptors leads to unopposed stimulation and worsening of hypertension.  $\beta$ -blockers with additional  $\alpha$ -blocking properties are synergistic with  $\alpha$ -blockers in reducing B.P. eg. labetalol (100-400mg/day) and carvedilol (12.5-50mg/day).

Calcium channel antagonists can be used for preoperative control of B.P. and reduce preoperative and intraoperative coronary spasm. Preoperative sedation and anxiolysis and assurance will decrease anxiety and prevent marked haemodynamic fluctuation in immediate preoperative period [1] [Table/Fig-6] [15].

Communication between operating and anaesthesia teams is crucial for success of intraoperative management of patients undergoing resection.

Routine monitoring along with CVP monitoring. Pulmonary artery catheter is not an absolute requirement and should be reserved for severe left ventricular dysfunction and cardiovascular compromise [16].

G.A. with thoracic epidural anaesthesia was chosen for our patient as thoracic epidural blocks, sensory and sympathetic discharge in

area of surgical field and hence, provides better haemodynamic stability.

Midazolam can be used to facilitate co-induction [11]. Anaesthesia can be induced with fentanyl 2-5 µg-1 and Propofol 1-2 mgkg-1.

Intubation should be attempted with satisfactory depth of anaesthesia. Vecuronium, Rocuronium and Cisatracurium have shown cardiovascular stability and release the least histamine. Atracurium and mivacurium release histamine.

To achieve intraoperative and postoperative analgesia by epidural route, infusion of bupivacaine 0.1-0.125% with fentanyl 2 mcgml-1 at the rate of 6-12 mlhr-1, is administered after an initial bolus of 8-10 ml of 0.25% bupivacaine in divided doses [1,10].

Sodium Nitroprusside (SNP), Phentolamine (boluses of 1-5 mg), Prazosin, Nitroglycerine (NTG) and various other agents like Magnesium Sulphate (loading dose of 40-60 mgkg-1 followed by 1-2 ghr-1), Nicardipine, Diltiazem, Esmolol are used to control rises in B.P. [1,4,10,13,18,19].

Lidocaine is useful for ventricular arrhythmias while Amiodarone is an alternative.

Volume loading before tumour ligation and fluid boluses should be tried before choosing adrenaline, noradrenaline and phenylephrine for Catecholamine withdrawal following venous ligation.

Patient is usually kept in ICU unit for first 24 hrs and monitored for haemodynamic instability [5,10,3,17]. Epidural analgesia provides good post-operative pain relief and may be supplemented by oral medications.

Approximately 50% patients remain hypertensive for few days, likely related to elevated catecholamine levels which persist for one week after resection [16].

## CONCLUSION

Pheochromocytoma is rare and can present with multitude of symptoms mimicking other diseases. Good preoperative preparation and the judicious use of a combination of vasodilatory and vasopressor medications help in reducing mortality and morbidity associated with surgery. Good communication between surgeon, endocrinologist and anaesthesiologist is crucial for the safe management of these patients.

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