CASE SERIES

A Retrospective Case Series on Planned and Accidental Pheochromocytoma Resection Surgery: Role of Preoperative Preparation

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Abstract

Successful anesthetic management of patients with adrenal tumors requires a well-orchestrated and multidisciplinary approach. We report the successful anesthetic management and outcomes of five rare cases of adrenal tumors in adult and pediatric patients. Careful attention was paid to patient hydration, and salt supplementation was concurrently administered. Pharmacological therapy was started and required investigations, optimization was done preoperatively, and patients were admitted 2–3 days before surgery. During surgery, pheochromocytoma requires keen vigilance, invasive monitoring, appropriate anesthetic techniques, and vasodilator use during the perioperative period to tackle hypertensive crisis; vasopressors may be required postoperatively. All patients were clinically stable after surgery and were successfully discharged.

Keywords: Anesthesia, Case report, Epinephrine, Norepinephrine, Paraganglioma, Pheochromocytoma.

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Introduction

Managing pheochromocytoma can pose a challenge for anesthesiologists, especially if it remains undetected. These tumors, composed of chromaffin tissue, are commonly encountered during anesthesia and their symptoms can differ greatly. Nevertheless, surgical management of these tumors has significantly improved over time due to advances in surgical techniques, diagnostic capabilities, and proper preoperative preparation. Ensuring an appropriate anesthetic approach during the perioperative period is crucial for achieving the best possible outcome. Collaboration among physicians from various specialties from the outset is essential for achieving optimal results.[1–4]

Case Series

We report five cases of pheochromocytoma at a tertiary care hospital in India. The study was done between February 2021 and March 2022. Pheochromocytoma diagnosis was confirmed by endocrinologists using biochemical testing (24-hour urine metanephrine and normetanephrine) and computed tomography (CT) imaging. The anesthesia team, cardiologists, neurologists, and nephrologists attended to the patients for optimization. All patients were made clinically stable under pharmacological therapy (phenoxybenzamine, calcium channel blockers, and β-blockers) before admission for elective surgery. Patients were also advised to take adequate fluids, a high salt diet, and antihypertensive medications. The patient regularly visited the outpatient department till admission, and serial hematocrit was measured to check the adequacy of fluid replacement (Table 1).

The patients were admitted 3 days before surgery. A high sodium diet (5000 mg/day) was initiated, and continuous saline infusion was given 2500 mL/day.

All the patients were operated under general anesthesia (GA) with a thoracic epidural, preferably at T11–12. After securing the intravenous (IV) lines, the standard American Society of Anesthesiologists (ASA) monitors were attached. Arterial and central venous lines were connected, and urinary catheterization was done. We preferred etomidate (0.2–0.3 mg/kg) as an induction agent and vecuronium as a muscle relaxant because of their hemodynamic stability and nonrelease of histamine. Injection fentanyl 100 µg was given during induction, and paracetamol 1000 mg was infused at the end of surgery for analgesia. Drugs that may increase catecholamine levels, like desflurane, ketamine, morphine, pethidine, atracurium, and metoclopramide, were avoided. Nitroglycerine (NTG), sodium nitroprusside (SNP), esmolol, and norepinephrine (NE) infusions were prepared and labeled correctly. Loading of dexmedetomidine (DEX)

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Patient consent statement: The author(s) have obtained written informed consent from the patients (for case 1, 2, 4 & 5) and the patient's parents (for case 3) for publication of the case report details and related images.

Table 1: Table showing demographic profile, medical history, drug history, CT scan findings, and laboratory investigations of patients

	Patient 1	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*
Age at presentation	56 years	35 years	12 years	45 years	45 years
Sex	Female	Male	Female	Female	Male
Genetic testing	Not done	Not done	Not done	Done Two of her three children had positive results and operated later on	Not done
Family history	No	No	No	No	No
Presenting symptoms	Nil	Generalized seizure	Chest pain, palpitation	Headache, abdominal pain, anxiety, and sweating	Severe pain abdomen
Other comorbidities (apart from hypertension)	None	Cerebrovascular accident	Concentric left ventricular hypertrophy	Type 2 diabetes mellitus, hypothyroidism	Left ventricular hypertrophy
Preoperative medication given	Prazosin 15 mg TDS Nifedipine 120 mg TDS Propranolol 40 mg OD	Prazosin 15 mg TDS Nicardipine 80 mg TDS Propranolol 40 mg OD Tab phenytoin 100 mg TDS	Tab torsemide 10 mg OD and tab carvedilol 6.25 mg BD	Tab prazosin 5 mg OD Tab thyroxine 50 µg OD metformin 500 mg and tab gliclazide 80 mg OD	Tab atenolol 50 mg BD
Location and size of tumor	Medial limb of right adrenal 29 × 29 × 35 mm	Right suprarenal region 38 × 22 × 28 mm	Left suprarenal fossa 45 × 34 × 35 mm	Left suprarenal fossa 4.7 × 12 × 14.1 mm with left paraaortic and aortocaval nodes (16.7 × 11.2 mm)	Some retroperitoneal mass was present, engulfing the inferior vena cava
Metastasis	_	_	_	_	_
Urinary metanephrine (24 hours)	942.80	220.68	281.82	423.65	Not done
Urinary normetanephrine (24 hours)	188.55	1754	2366.27	234.56	Not done

BD, twice a day; OD, once a day; TDS, thrice a day

was given at the rate of 1 µg/kg for 10 minutes, followed by an infusion of 0.5 µg/kg in all patients till resection of the tumor. Blood sugar was measured at induction and after that at every hour interval. In the postoperative period, blood sugar was measured every 3 hours for 24 hours. We also used bispectral index (BIS) monitoring to maintain deeper planes of anesthesia throughout the intraoperative period. The epidural infusion was started with 0.25% bupivacaine at the rate of 5 mL/hour, and anesthesia was maintained on 50% oxygen, nitrous oxide, and sevoflurane with an intermittent dose of vecuronium. CVP-guided adequate amounts of fluid and blood products were administered. The epidural infusion was stopped after tumor resection, but the catheter was kept in place for postoperative pain relief. However, intraoperative management was different in all patients (Figs 1 to 3).

Patient one was a 56-year-old woman who was incidentally diagnosed with pheochromocytoma on CT. Preoperatively, she was optimized with tablet (tab) prazosin 15 mg thrice a day (TDS), tab nifedipine 120 mg TDS, and tab propranolol 40 mg once a day (OD). A loading infusion of 500 µg/kg of esmolol and DEX 1 µg/kg over 10 minutes was initiated before induction to overcome the sympathetic response during intubation. The DEX dosage was adjusted intraoperatively according to hemodynamic variations and discontinued after tumor resection. After intubation, NTG was also started at 5 µg/kg/minute and increased to 10 µg/kg/minute during tumor manipulation. Still, blood pressure (BP) kept rising and increased to 200/110 mm Hg. Esmolol was continued at

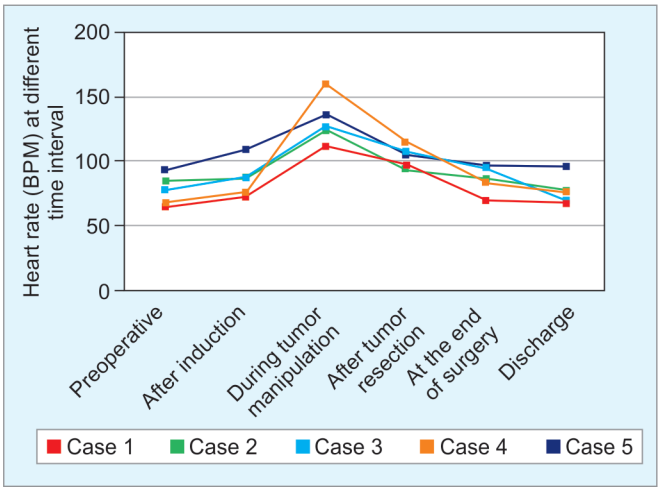

Fig. 1: Heart rate of the patients at different time intervals

100–150 µg/kg/minute. Still, BP kept growing. Finally, BP could be controlled after adding SNP at 0.5 µg/kg/minute. DEX and other antihypertensive medications were tapered and stopped after tumor resection; NE infusion was initiated at 10 µg/minute, and gradually tapered to 8 µg/minute to maintain mean arterial pressure above 65 mm Hg. The patient was observed for 15 minutes postoperatively. Her BP was 112/73 mm Hg when she

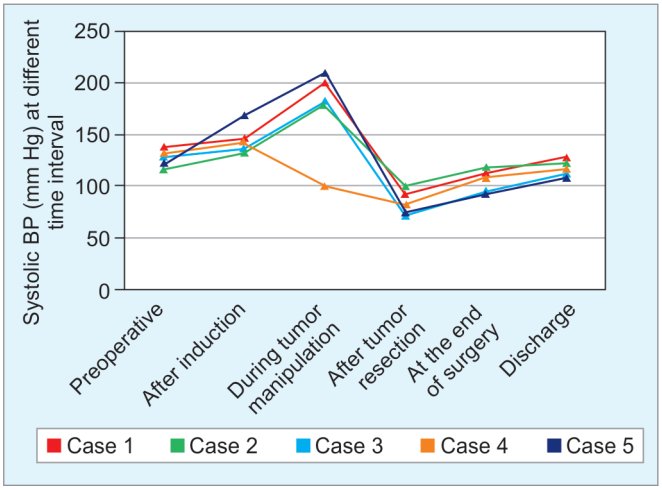

Fig. 2: Systolic BP of patients at different time intervals

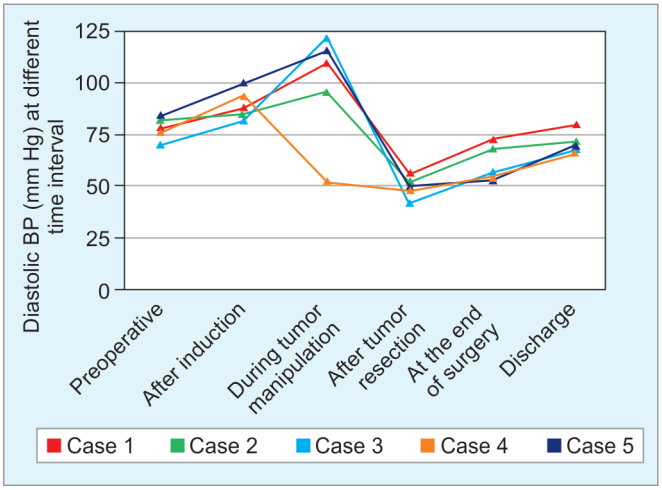

Fig. 3: Diastolic BP of patients at different time intervals

was moved to the postoperative ward with an epidural infusion of 0.125% bupivacaine with fentanyl at 1–2 µg/mL for postoperative pain relief. The NE infusion was tapered gradually over 6 hours. She was followed up for 3 days and eventually discharged.

Patient two was a 35-year-old man with right pheochromocytoma, and he was taking tab phenytoin 100 mg TDS, tab nicardipine 80 mg TDS, tab prazosin 15 mg TDS, and tab propranolol 40 mg OD for 1 week. Intraoperatively, he received a loading infusion of esmolol (500 µg/kg) and DEX (1 µg/kg) for 10 minutes. Intraoperatively, BP was managed further with NTG (8–10 µg/kg/minute) and esmolol (100–150 µg/kg/minute). The intraoperative period was uneventful. About 2 L of fluid was administered before tumor resection. No hypotension was observed after tumor resection. The patient was discharged on the 10th postoperative day (Fig. 4).

The third patient was a 12-year-old girl scheduled for an open left adrenalectomy. She was diagnosed with hypertension and admitted to the pediatric intensive care unit (ICU) for 2 days. Here, labetalol infusion was initiated for BP regulation. She was later diagnosed with pheochromocytoma and started on tab torsemide 10 mg OD and carvedilol. Two-dimensional echocardiography revealed an ejection fraction of 70% with concentric left ventricular hypertrophy. The patient was wheeled into the operation theater (OT), standard monitoring was attached, and a DEX bolus was administered (1 µg/kg over 20 minutes), followed by infusion at 0.5 µg/kg/minute. The anesthetic management was like other patients. However, 7 mL, 0.25% ropivacaine was given as a bolus through an epidural catheter instead of an infusion. After induction, NTG infusion was initiated (10–12 µg/minute). During tumor manipulation, the patient's BP suddenly increased (182/122 mm Hg). Simultaneously, SNP infusion was also started. The pulse rate also started rising (120–130 bpm). Esmolol infusion was started at 100 µg/kg/minute. Antihypertensive infusions were stopped after tumor resection. Still, her BP suddenly dropped (71/42 mm Hg), and NE infusion was started at 12 µg/minute. BP kept falling, so vasopressin infusion was started. When vital parameters were acceptable, the patient was moved to the postoperative high-dependency unit with NE infusion, gradually tapered over the next 12 hours. She was discharged on the 12th postoperative day with follow-up advice.

Patient four was a 45-year-old woman with a six-year history of hypertension. She was taking amlodipine 10 mg OD and atenolol 25 mg BD. She also had hypothyroidism during this period (treatment—tab thyroxine 50 µg). She had recently been diagnosed with type 2 diabetes mellitus (treatment—metformin 500 mg and tab gliclazide 80 mg). On presentation, the physician discontinued amlodipine and atenolol, and she has been initiated on tab prazosin 2.5 mg OD, which was increased to 5 mg OD. Adrenal myelolipoma was diagnosed on abdominal contrast-enhanced CT. In theater, BP was maintained with NTG, SNP, and esmolol. A CVP-guided total of 2800 mL of fluid was administered for 3.5 hours of surgery with 500 mL blood loss and 400 mL urine output. After 2 hours, during tumor resection, the patient developed ventricular tachycardia. The surgeons were asked to wait for a while till the return of normal sinus rhythm. Injection lidocaine was given at 1.5 mg/kg, repeated with 0.75 mg/kg after 10 minutes. The patient's BP and pulse rate were stabilized. After tumor resection, sudden hypotension was managed with NE infusion. The patient was transferred to the postoperative ward with NE infusion, discontinued after 2 hours.

The fifth patient was different from others as he was posted for excision of a retroperitoneal mass engulfing the inferior vena cava. He has had diabetes for 5 years and was on insulin therapy. He was also hypertensive, for which he was taking Tab atenolol, and his BP charting was normal. Echocardiography revealed left ventricular hypertrophy, and all other parameters were normal. It was posted as a routine case. As soon as the patient was induced, BP started shooting up. NTG, SNP, and esmolol infusion were started, and BP could be controlled. But as soon as the tumor was touched, BP again started rising. An intermittent bolus of labetalol and a bolus dose of magnesium sulfate was also given. After that, sudden hypotension was observed. Now it was suspected that the mass could be pheochromocytoma. CVP line, arterial line, and transesophageal Doppler were connected. A large fluid bolus was given through CVP. Recurrent episodes of hypotension and hypertension were managed with continuously adjusting infusion of antihypertensive drugs and NE. Surgeons carefully resected the tumor, and all antihypertensive infusions were stopped. However, the patient was shifted to ICU with the infusion of NE and vasopressin. Extubation was done the following day after vitals were stabilized. Histopathology later confirmed the diagnosis of pheochromocytoma (Fig. 5).

Discussion

The determination of plasma-free metanephrines and the determination of urinary fractionated metanephrines are equally

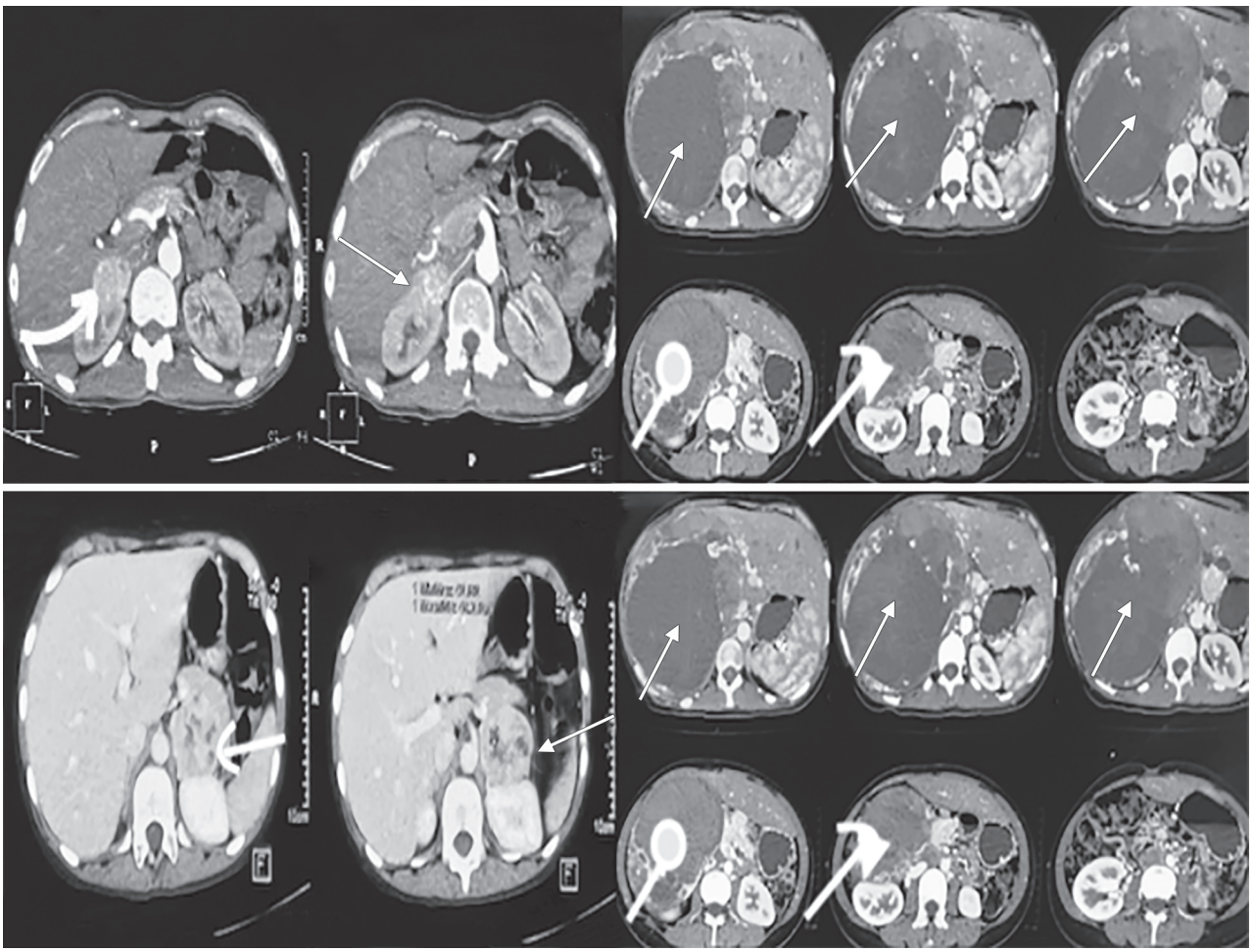

Fig. 4: CT of patient two

acceptable methods for the diagnosis of pheochromocytoma and the choice of one method over the other is debatable. Endocrinologists in our institution measured 24 urine urinary metanephrine and normetanephrine for biochemical confirmation of pheochromocytoma and CT imaging was done thereafter.[5,6]

Reasonable preoperative pharmacological control, control of adverse effects of circulatory catecholamine, and restoration of intravascular volume are critical to good perioperative outcomes. Endocrine Society of Clinical Practice guidelines recommend a high salt diet and fluid intake to reverse catecholamines-induced blood volume contraction preoperatively and to prevent severe hypotension after tumor resection.[7] Combined general and regional anesthesia was the technique of choice, and this was used in all patients.[8] Per recommendations, standard and invasive monitoring (invasive BP and CVP) and BIS were used in all cases. Response to endotracheal intubation were suppressed using a DEX bolus before induction. More profound anesthesia was maintained through the procedure guided by (BIS) monitoring.

Hypertensive crisis during tumor manipulation was managed with potent, short-acting vasodilators NTG and esmolol.[9–13] Each patient required a different dose/combination of antihypertensive medications. Labetalol and magnesium sulfate are also effective agents to reduce blood pressure, and they were used only in our fifth patient.

Vasopressors are required immediately after removing the tumor to control sudden hypotension. A large-volume fluid bolus was administered immediately before tumor ligation to prevent severe hypotension. Noradrenaline infusion and vasopressin infusions were used to treat hypotension postoperatively. Sometimes adrenaline in 1:10 dilution or vasopressin drip is needed in emergencies if hypotension is not corrected, but it was not required in our cases. Some researchers have used methylene blue for severe hypotension after tumor ligation.[14]

Excess catecholamine in these patients can induce or aggravate insulin resistance, and hypoglycemia is a frequent complication of pheochromocytoma resection. Therefore, we monitored blood glucose levels throughout the perioperative period.[15]

Pheochromocytoma is associated with various syndromes and, therefore should be investigated thoroughly. Theodosopoulou et al. reported a patient with type 1 neurofibromatosis (NF-1) presented for myomectomy. The patient developed a hypertensive crisis during anesthesia due to an occult pheochromocytoma managed by infusion of NTG. Surgery was not done, and the patient was reversed. They suggested a thorough investigation of NF-1 patients before elective surgery due to the diversity of the disease's clinical manifestations. A similar incident happened with our fifth patient, who was not diagnosed with pheochromocytoma preoperatively and was posted as simple laparotomy, and managing the BP remained challenging for us throughout the perioperative period.[16]

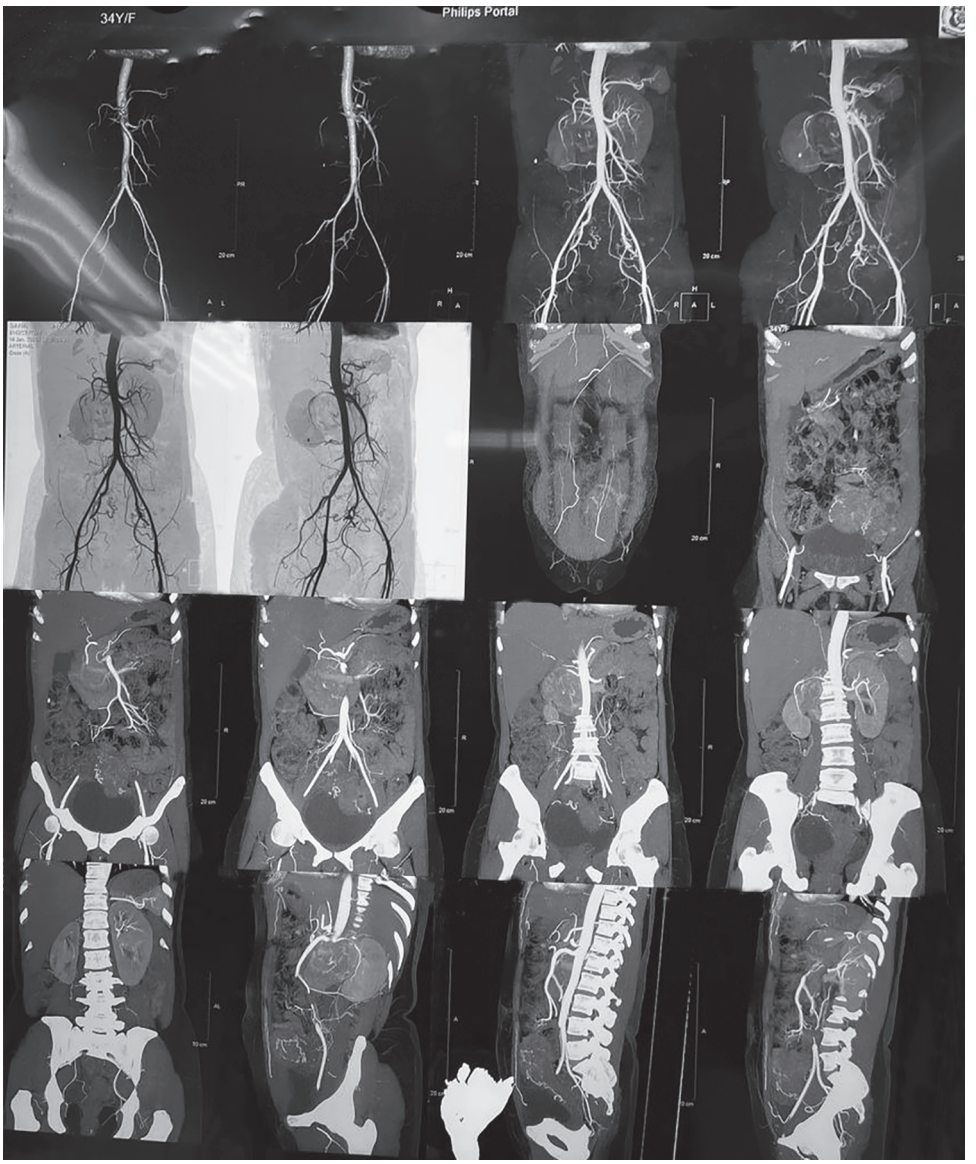

Fig. 5: Abdominal CT of patient five

Imbelloni et al. published a case series of three pheochromocytoma cases. They used SNP, NTG, phentolamine bolus, and magnesium sulfate for the hypertensive crisis. All cases were done under GA + epidural. They stressed that effective preoperative control of blood pressure, a multidisciplinary approach, and good teamwork is very important for a good outcome in reducing morbidity and mortality.[17]

Conclusion

Definitive treatment of pheochromocytoma consists of surgical removal. The complications in these patients can be effectively reduced by adequate preoperative pressure control, preoperative fluid restoration, optimization of cardiovascular status, and adequate use of antihypertensive and vasopressor drugs during surgery. Strict hemodynamic control of the patient in OT and ICU is recommended. Coordinated efforts by surgical, medical, and anesthesia teams led to the discharge of all patients successfully from the hospital.

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References

1. Lenders JW, Eisenhofer G, Mannelli M, et al. Phaeochromocytoma. Lancet 2005;366(9486):665–675. DOI: 10.1016/S0140-6736(05)67139-5
2. Pacak K, Wimalawansa SJ. Pheochromocytoma and paraganglioma. Endocr Pract 2015;21(4):406–412. DOI: 10.4158/EP14481
3. Lam AK. Update on adrenal tumours in 2017 World Health Organization (WHO) of endocrine tumours. Endocr Pathol 2017;28(3):213–227. DOI: 10.1007/s12022-017-9484-5
4. Wang W, Zhou H, Sun A, et al. Anesthetic management of a giant paraganglioma resection: a case report. BMC Anesthesiol 2022;22(1):212. DOI: 10.1186/s12871-022-01766-7

5. Eisenhofer G, Lenders JW, Pacak K. Biochemical diagnosis of pheochromocytoma. Front Horm Res 2004;31:76–106. DOI: 10.1159/000074659
6. Därr R, Kuhn M, Bode C, et al. Accuracy of recommended sampling and assay methods for the determination of plasma-free and urinary fractionated metanephrines in the diagnosis of pheochromocytoma and paraganglioma: a systematic review. Endocrine 2017;56(3): 495–503. DOI: 10.1007/s12020-017-1300-y
7. Nölting S, Bechmann N, Taieb D, et al. Personalized management of pheochromocytoma and paraganglioma. Endocrine Reviews 2022;43(2):199–239. DOI: 10.1210/endrev/bnab019
8. Yang M, Kang C, Zhu S. Effects of epidural anaesthesia in pheochromocytoma and paraganglioma surgeries: a protocol for systematic review and meta-analysis. Medicine (Baltimore) 2022;101(47):e31768. DOI: 10.1097/MD.0000000000031768
9. Berends AMA, Kerstens MN, Lenders JWM, et al. Approach to the patient: perioperative management of the patient with pheochromocytoma or sympathetic paraganglioma. J Clin Endocrinol Metab 2020;105(9):dgaa441. DOI: 10.1210/clinem/dgaa441
10. Gruber LM, Jasim S, Ducharme-Smith A, et al. The role for metyrosine in the treatment of patients with pheochromocytoma and paraganglioma. J Clin Endocrinol Metab 2021;106(6): e2393–e2401. DOI: 10.1210/clinem/dgab130
11. Connor D, Boumphrey S. Perioperative care of phaeochromocytoma. BJA Education 2016;16(5):153–158. DOI: 10.1093/bjaed/mkv033
12. Araujo-Castro M, Pascual-Corrales E, Nattero Chavez L, et al. Protocol for presurgical and anaesthetic management of pheochromocytomas and sympathetic paragangliomas: a multidisciplinary approach. J Endocrinol Invest 2021;44(12):2545–2555. DOI: 10.1007/s40618-021-01649-7
13. Naranjo J, Dodd S, Martin YN. Perioperative management of pheochromocytoma. J Cardiothorac Vasc Anesth 2017;31(4): 1427–1439. DOI: 10.1053/j.jvca.2017.02.023
14. Amin Nasr A, Fatani J, Kashkari I, et al. Use of methylene blue in pheochromocytoma resection: case report. Paediatr Anaesth 2009;19(4):396–401. DOI: 10.1111/j.1460-9592.2009.02956.x
15. Ronen JA, Gavin M, Ruppert MD, et al. Glycemic disturbances in pheochromocytoma and paraganglioma. Cureus 2019;11(4):e4551. DOI: 10.7759/cureus.4551
16. Theodosopoulou P, Nastos C, Paraskeva A. Anesthetic management of a patient with type 1 neurofibromatosis and an occult pheochromocytoma: a case report. Braz J Anesthesiol 2023 73(5):695–698. DOI: 10.1016/j.bjane.2021.02.045
17. Imbelloni LE, Lemos Neto SV, Rivoli ALC, et al. Anesthetic management for patients with pheochromocytoma: series of three cases. Japanese J Gstro Hepato 2021;8(2):1–4