

Pheochromocytoma is a rare neuroendocrine tumor – Two case Report

Abstract

Pheochromocytoma is a hormone secreting benign neuroendocrine tumor of adrenal medulla containing chromaffin cells. These cells are located in the medulla of an adrenal gland, they release certain hormones, mainly epinephrine(adrenaline) and norepinephrine(non-adrenaline). When a pheochromocytoma the tumor releases hormones that causes, high blood pressure, headache, hyperhidrosis and symptoms of a panic attacks or spells. Adrenaline and noradrenaline triggers the body fight or flight response. Usually pheochromocytoma affects only one adrenal gland but it can affect both glands. 90% pheochromocytoma are benign tumour but 10% pheochromocytoma may be malignant. Pheochromocytoma occur more often age between 30 and 50 years of age. Approximately 25 to 35% of people have a hereditary condition such as multiple endocrine neoplasia type II syndrome, Van-Hippel- Liandu syndrome and neurofibromatosis type I.

chromaffin cell tumor located outside of the adrenal glands are called paragangliomas, which causes same effects on the body as a pheochromocytoma. Surgical resection is the main treatment for pheochromocytoma.

We are reporting two rare cases of pheochromocytoma in a 30 years female and 60 years male, having symptoms of high blood pressure, headache and hyperhidrosis. Diagnosis of pheochromocytoma was confirmed by CT abdomen, 24-hour urine test and blood catecholamine test. Female patient was treated by open adrenalectomy and Male patient was performed laparoscopic adrenalectomy.

Key words

Pheochromocytoma, Adrenal medulla, Chromaffin cell, Paraganglioma, Neuroendocrine tumor

Introduction

Pheochromocytomas are benign tumours that originate from chromaffin cells in the adrenal medulla. The annual incidence rate of pheochromocytoma ranges from 2 to 8 cases per 100,000 individuals. Approximately 25-35% of cases are associated with genetic conditions such as multiple endocrine neoplasms type 2A and 2B, Von Hippel-Lindau syndrome, and neurofibromatosis type I. [1,2]

Clinical manifestations of pheochromocytoma, often summarized by the "5 Hs," include hypertension, headache, hyperhidrosis, hyperglycaemia, and hypermetabolism. The "Rule of 10s" highlights various aspects of pheochromocytoma, including 10% of patients having malignant

disease, 10% bilateral adrenal disease, 10% extra-adrenal disease, 10% familial inherited disease, 10% occurrence in children, 10% recurrence in 5 to 10 years, 10% absence of hypertension, and 10% presence of calcification on CT. [1,3,4]

Symptoms of pheochromocytoma include high blood pressure, headache, hyperhidrosis, palpitations, anxiety, weight loss, and gastrointestinal disturbances. These symptoms may manifest suddenly in spells or attacks triggered by physical exertion, stress, changes in body position, surgery, anaesthesia, certain medications, and specific foods and stimulants. [1,2]

Paragangliomas, which are extra-adrenal pheochromocytomas, can develop in various locations such as the sympathetic chain, aorta, carotid body, organs of Zuckerkandl, genitourinary system, pericardium, and dermoid cysts. Around 20-40% of paragangliomas are malignant. [4,5,6]

Diagnostic approaches for pheochromocytoma include clinical presentation, biochemical tests measuring plasma and urinary metanephrines, 24-hour urine tests for catecholamines and Vanillylmandelic Acid (VMA), blood catecholamine tests, genetic counselling for hereditary syndromes, and imaging methods such as ultrasonography, CT scans, MRI, and PET/CT scans. [1,4]

CT scans are often considered the gold standard for diagnosing pheochromocytoma due to their high accuracy in detecting tumours, although PET/CT scans are preferred for detecting both pheochromocytomas and paragangliomas. [4,5]

Case Report

Case I

A 30-year-old female presented to our centre on October 25, 2015, complaining of headache, hypertension, and intermittent palpitations with tachycardia. Upon physical examination, her blood pressure was recorded as 210/110. Investigation revealed a suspicion of pheochromocytoma. A CT scan of the abdomen showed a left adrenal tumor measuring 10x10 cm, spherical in shape, with a smooth regular margin and central necrosis, confirming the diagnosis of pheochromocytoma of the left adrenal gland. Biochemical analysis revealed elevated levels of plasma catecholamines, 24-hour urinary catecholamines, and vanillylmandelic acid (VMA) above normal values.

Preoperatively, symptoms of hypertension were managed with oral Alpha-blockers initiated 14-15 days before surgery, along with control of tachycardia achieved through β -blockers and calcium channel blockers. The patient's blood pressure was controlled at 120/80, and her heart rate was maintained between 60-80 beats per minute.

Operative management was carried out collaboratively by anaesthesiologists and surgeons. Due to the large size (10x10 cm) of the pheochromocytoma, open surgery was planned. Preoperative anxiety was alleviated with diazepam, and atropine was avoided. Direct muscle relaxants were administered for intubation. During intubation and surgery, hypertensive crises were promptly managed with intravenous nitroprusside, and arrhythmias were controlled with lidocaine.

An open surgical approach with a midline incision allowed complete exposure and inspection of the left adrenal gland. The adrenal vein was identified and clipped, and remaining soft tissue attachments were divided, leading to successful total left adrenalectomy. The patient's postoperative course was uneventful, with monitoring of blood pressure, volume status, and blood sugar for the first 24 hours. Postoperatively, blood pressure remained controlled, and the patient was discharged on the 10th postoperative day. After 5-year follow-up, the patient remained healthy with no recurrence.

On gross examination, the tumor appeared spherical with regular margins and weighed 200 grams. Histopathological analysis confirmed the presence of benign pheochromocytomas containing small nests of chromaffin cells with eosinophilic cytoplasm. (Fig 1-8)



Fig-1 CT abdomen showed a 10x10 cm cystic lesion on left side above the kidney, A pheochromocytoma

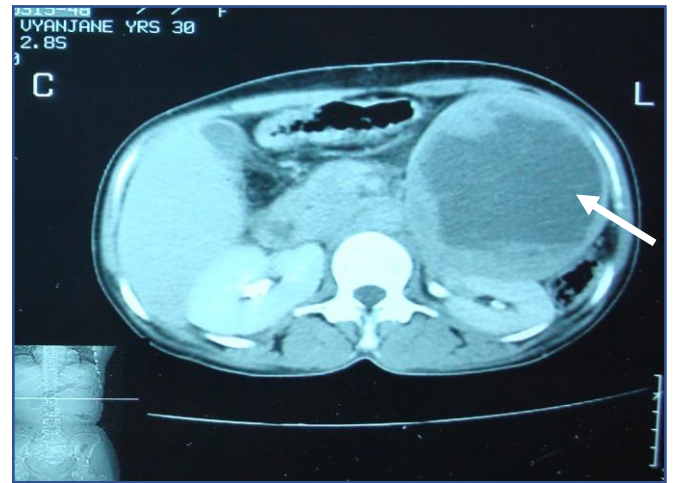


Fig-2 CT abdomen showed a spherical, regular margin tumor with central necrosis

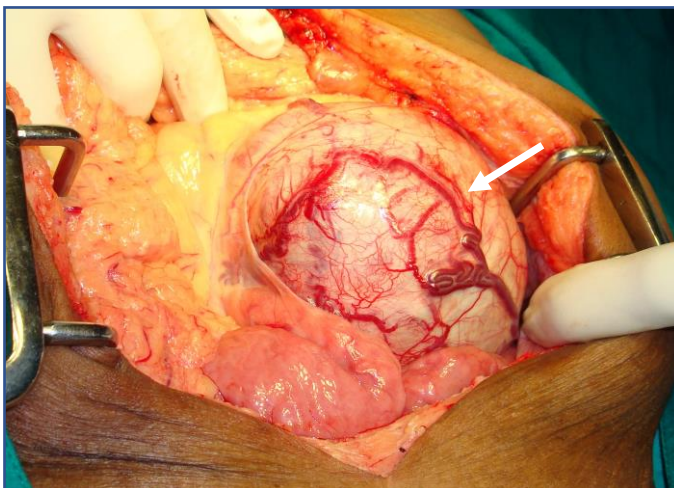


Fig-3 Intra operative photographs a big cystic lesion above the left kidney

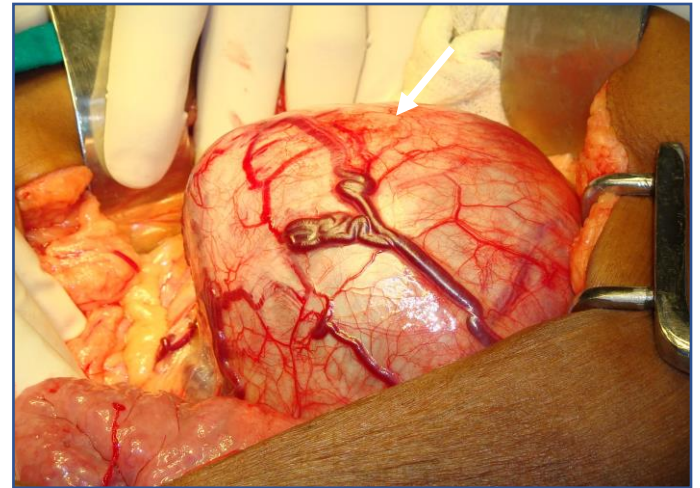


Fig-4 Intra operative photographs a big cystic lesion above the left kidney

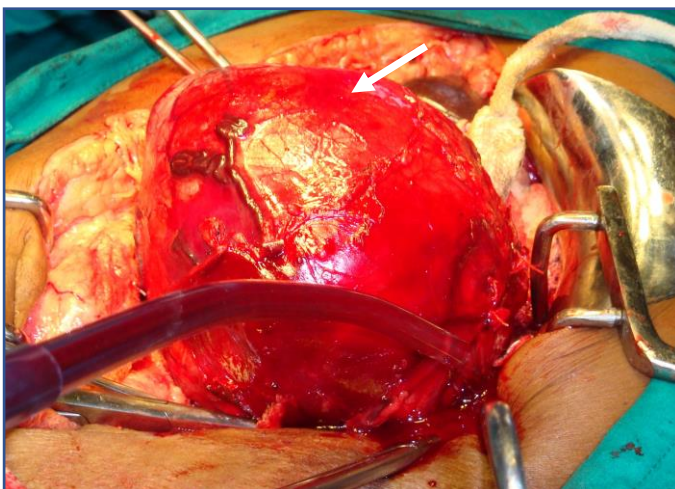


Fig-5 Intra operative photographs showing resection of left adrenal tumor

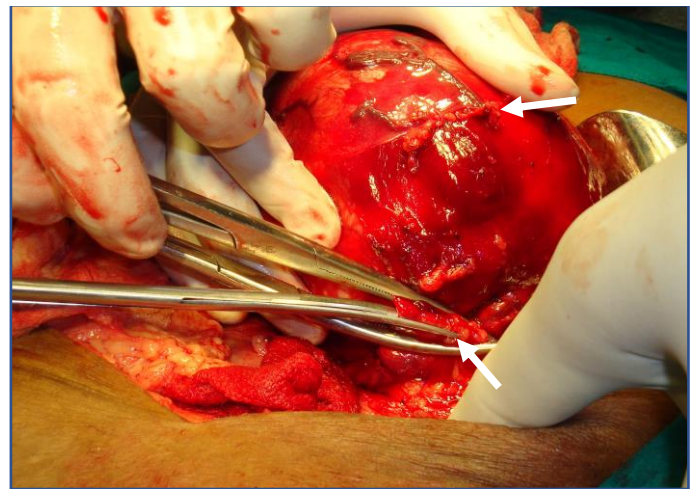


Fig-6 Intra operative photographs showing left adrenal vein ligation. "vein first technique"

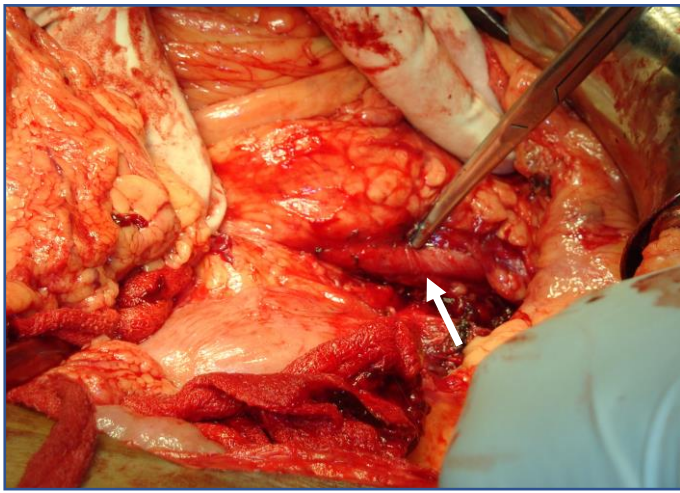


Fig-7 Intra operative photographs showing aorta with total left adrenalectomy.

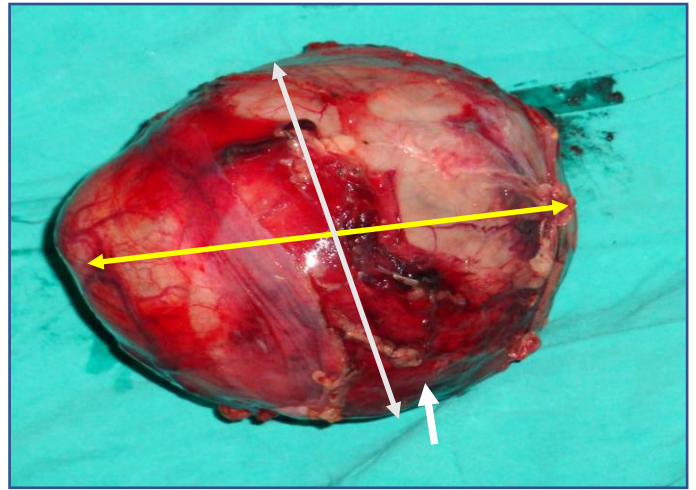


Fig-8 Gross specimen measuring 10x10 cm benign pheochromocytoma

Case II

A 60-year-old male was admitted to our centre on June 27, 2021, presenting with a history of headaches, hypertension, and abdominal pain over the past 5 years. Evaluation for pheochromocytoma was initiated. A CT scan of the abdomen revealed a 5x3 cm, oval-shaped mass on the right adrenal gland. On examination, his blood pressure was elevated at 230/110, and ECG showed tachycardia without cardiac arrhythmias. Biochemical investigations revealed elevated plasma and urinary catecholamines.

Preoperative management involved initiating Alpha-blocker therapy 15 days before surgery to control blood pressure. Beta-blockers were added three days prior to surgery to manage tachycardia. Intravascular volume expansion was achieved with the infusion of 1 liter of crystalloid solution.

Laparoscopic surgery was planned and surgical technique involved placing the patient in a lateral decubitus position with a trans-peritoneal approach. Three right subcostal ports were utilized, with one 10 mm port for the camera at the umbilicus and a 5 mm port placed in the subxiphoid position for liver retraction. A diagnostic laparoscopy was initially performed to rule out malignancy. The right hepatic lobe was mobilized completely to facilitate visualization and safe access to the vena cava and adrenal vein. The right adrenal vein was exposed and safely clipped after developing a plane between the vena cava and the medial margin of the adrenal gland. The adrenal gland was dissected away from the retroperitoneum on both sides.

Utilizing the "vein first technique," the main adrenal vein was identified, dissected, and divided between clips. Harmonic bipolar forceps were used for adrenal gland dissection, followed by total adrenalectomy. A surgical specimen measuring 5x3 cm and oval in shape was extracted through a mini-laparotomy site, and a drainage tube was placed for 2 days. Postoperatively, the patient's recovery was uneventful, and blood pressure remains controlled. The patient was discharged on the 5th postoperative day without complications. Histopathological examination confirmed the presence of a benign pheochromocytoma. After 3-year follow-up, the patient's condition healthy, without recurrence. **(Fig 7-14)**

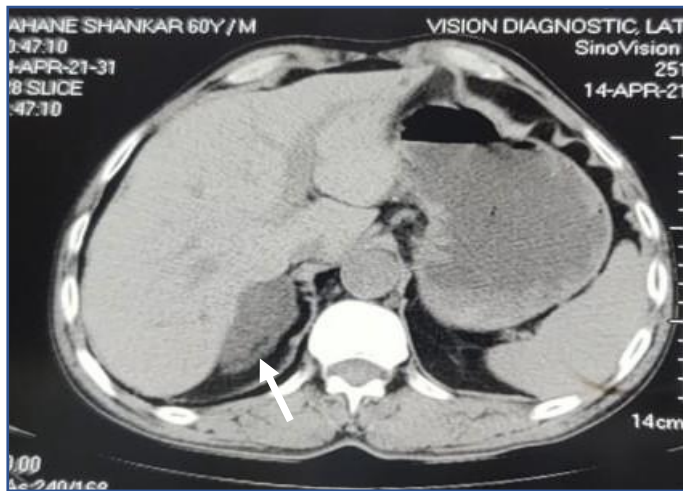


Fig-7CT abdomen showed a 5x3 cm SOL lesion on right side, above the kidney, A pheochromocytoma

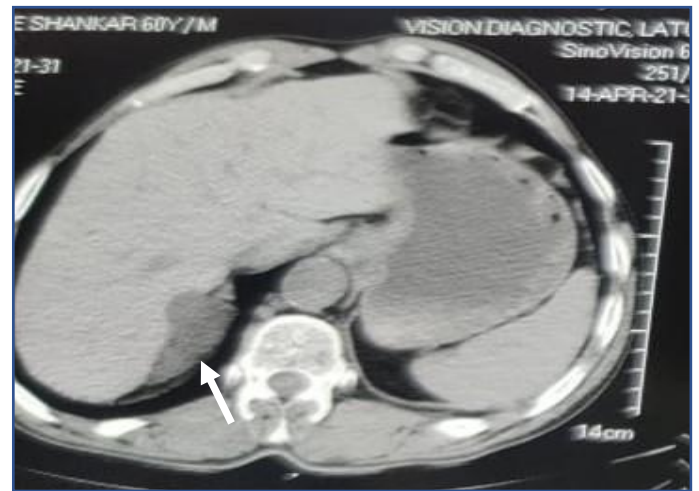


Fig-8CT abdomen showed a 5x3 cm SOL lesion on right side, above the kidney, A pheochromocytoma

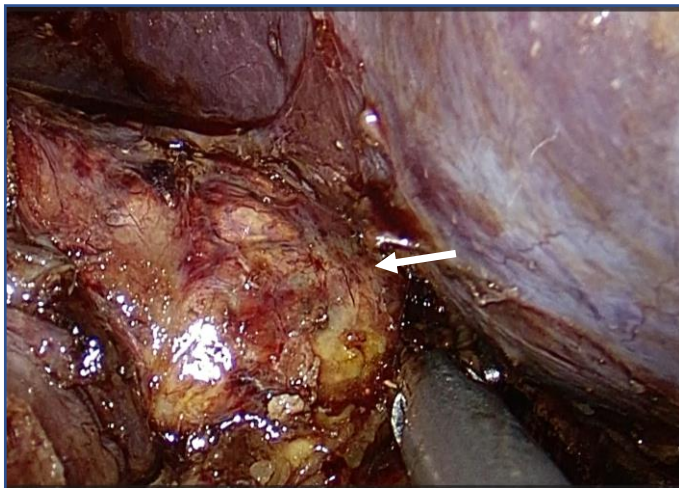


Fig-9Intra operative Laparoscopic photographs showing right side adrenal tumor



Fig-10 Intra operative Laparoscopic photographs showing right side adrenal tumor of size 5x3 cm



Fig-11 Intra operative Laparoscopic photographs showing total excision of size right adrenal tumor

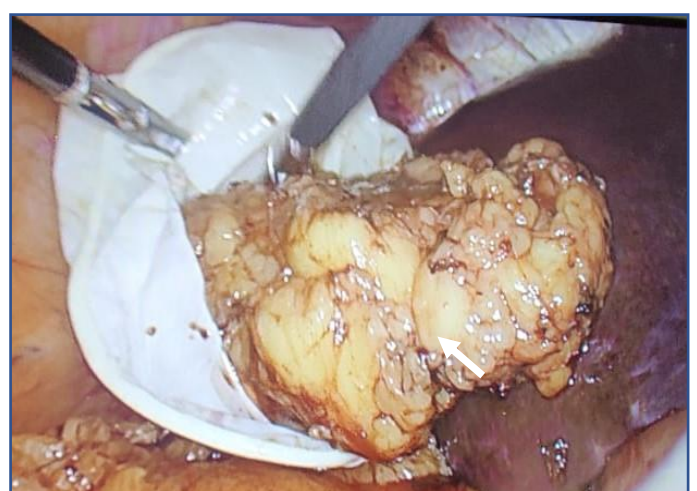


Fig-12 Intra operative Laparoscopic photographs showing right side adrenal tumor with extraction bag

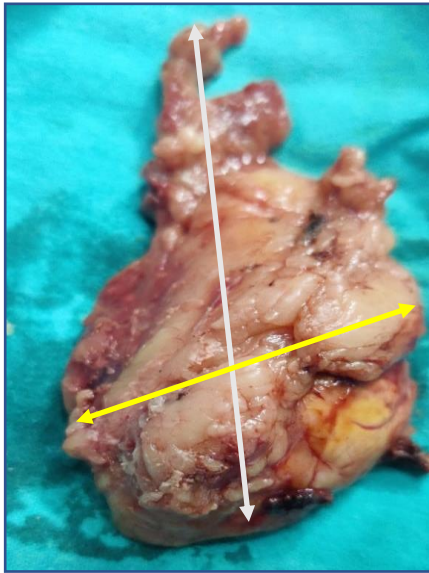


Fig-13 Gross specimen measuring 5x3 cm right pheochromocytoma

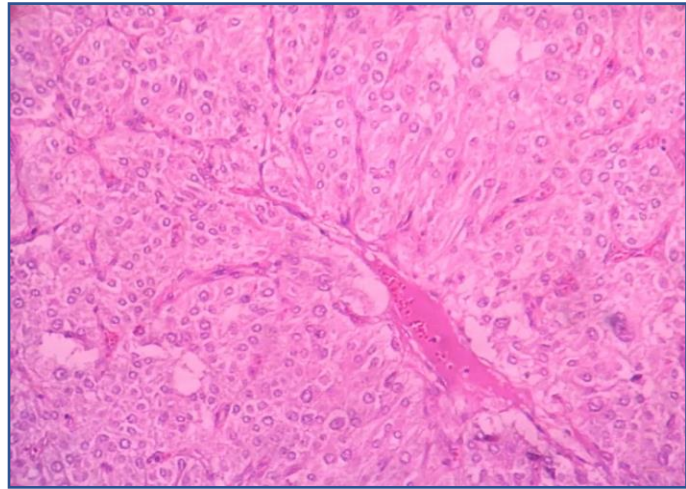


Fig-14 Histopathology showing Pheochromocytoma tumor with chromaffin cells

Discussion

Professor Ludwig Pick, a German physician, first coined the term "pheochromocytoma" in 1912. Pheochromocytoma, a benign tumor of the adrenal medulla secreting catecholamines in 90% of cases, manifests with symptoms such as headache, palpitations, swelling, and hypertension in approximately 90% of patients. The gold standard imaging modality for identifying adrenal pheochromocytomas is CT abdomen, which identifies 95% of these tumors. [1,2,4,]

Surgical management of pheochromocytoma requires a multidisciplinary team comprising endocrinologists, surgeons, and anaesthesiologists experienced in managing the condition. Preoperative goals include optimizing blood pressure and normalizing intravascular volume. Adequate preoperative blood pressure control targets a systolic/diastolic blood pressure of 120/80 mmHg and a heart rate of 60-80 beats per minute. Patients are encouraged to maintain hydration with a high-sodium diet before surgery. [4,5,6]

Preoperative hypertension control involves alpha-blockers initiated 10-14 days before surgery, increased oral or intravenous fluid intake, and the addition of beta-blockers to manage tachycardia. Calcium channel blockers may also be used to control hypertension. Adequate blood pressure control minimizes hypertensive crises during surgery, reduces adverse effects of anesthesia, and maintains stable blood pressure intraoperatively. [1,2,3]

During anesthesia and intraoperative management, an experienced team should be prepared to manage hemodynamic functions with intravenous vasopressors. Patients may receive anti-anxiety medication such as midazolam, while atropine should be avoided. Propofol is commonly used for anesthesia induction, with muscle relaxants administered before endotracheal intubation to minimize a hypertensive response. Central venous access may be placed in patients with poor left ventricular function, and vasopressin infusion may be used to maintain blood pressure in hypotensive states. [5,6,7,8]

Intraoperative hypertensive crises are managed with intravenous nitroprusside, phentolamine, or nitro-glycerine, while arrhythmias are controlled with esmolol or lidocaine. Adequate volume replacement is essential to prevent postoperative hypertension, and calcium channel blockers may be used as primary therapy for blood pressure control. [2,3]

Surgical management options for pheochromocytoma include open adrenalectomy and laparoscopic adrenalectomy. Open surgery is preferred for large tumors (>6-12 cm), tumors in difficult-to-access locations, or suspected malignancy. Laparoscopic adrenalectomy, introduced in 1996 by Ganger et al, offers shorter hospital stays and minimal operative morbidity and mortality, making it safe and effective for managing pheochromocytoma irrespective of tumor size. [4,6,9]

Postoperative management involves close observation in the surgical ICU, with management of hypotension and hypertension as needed. Hourly blood sugar monitoring and prompt treatment of hypoglycemia are essential, while long-term survival rates following surgical removal of benign pheochromocytomas are high, with most patients becoming normotensive postoperatively. [2,3,10]

Conclusion

Pheochromocytoma, a rare tumor secreting catecholamines in 90% of cases, typically requires complete surgical removal as the definitive treatment. The gold standard for diagnosing pheochromocytoma involves using CT abdomen imaging and measuring elevated plasma free metanephrines through biochemical testing.

In cases of benign pheochromocytoma, the preferred approach is minimally invasive laparoscopic or robotic adrenalectomy. However, for larger tumors exceeding 6-12 cm or those of benign or malignant nature, open surgery remains the gold standard procedure.

Given the complexities involved, effective pheochromocytoma management necessitates the expertise of an endocrinologist, surgeon, and anaesthesiologists. Thus, a multidisciplinary team is essential to ensure the safety and success of pheochromocytoma surgery.

Reference

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