UNDER PEER REVIEW

Pheochromocytomaisarareneuroendocrinetumor: About TwocaseReports

Abstract

Pheochromocytoma is a hormone secreting benign neuroendocrine tumor of adrenal medullacontaining chromaffin cells. These cells are located in the medulla of an adrenal gland, they releasecertain hormones, mainly epinephrine(adrenaline) and norepinephrine(non-adrenaline). When apheochromocytoma the tumor releases hormones that causes, high blood pressure, headache,hyperhidrosis and symptoms of a panic attacks or spells. Adrenaline and noradrenaline triggers thebody fight or flight response. Usually, pheochromocytoma affects only one adrenal gland but it canaffect both glands. 90% pheochromocytoma are benign tumourbut 10% pheochromocytoma maybe malignant.Pheochromocytoma occurmoreoften agebetween30and50yearsof age.Approximately 25 to 35% of people have a hereditary condition such as multiple endocrine neoplasiatype IIsyndrome,Van-Hippel- Liandusyndrome andneurofibromatosistype I. Chromaffin cell tumor located outside of the adrenal glands are called paragangliomas, whichcauses same effects on the body as a pheochromocytoma. Surgical resection is the main treatmentforpheochromocytoma.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 ofpheochromocytoma was confirmed by CT abdomen, 24-hour urine test and blood catecholaminetest. Female patient was treated by open adrenalectomy and Male patient was performedlaparoscopicadrenalectomy.

Keywords: Pheochromocytoma,Adrenalmedulla,Chromaffincell,Paraganglioma,Neuroendocrinetumor

Introduction

Pheochromocytomas are benign tumours that originate from chromaffin cells in the adrenalmedulla. The annual incidence rate of pheochromocytoma ranges from 2 to 8 cases per 100,000individuals. Approximately 25-35% of cases are associated with genetic conditions such as multipleendocrine 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," includehypertension, headache, hyperhidrosis, hyperglycaemia, and hypermetabolism. The "Rule of 10s"highlightsvariousaspectsofpheochromocytoma,including10%ofpatientshavingmalignant

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%presenceofcalcificationonCT.[1,3,4]

Symptoms of pheochromocytoma include high blood pressure, headache, hyperhidrosis,palpitations, anxiety, weight loss, and gastrointestinal disturbances. These symptoms may manifestsuddenly in spells or attacks triggered by physical exertion, stress, changes in body position, surgery,anaesthesia,certainmedications, andspecificfoods andstimulants.[1,2]

Paragangliomas, which are extra-adrenal pheochromocytomas, can develop in various locationssuch as the sympathetic chain, aorta, carotid body, organs of Zuckerkandl, genitourinary system,pericardium,anddermoidcysts. Around20-40%ofparagangliomasare malignant. [4,5,6]

Diagnostic approaches for pheochromocytoma include clinical presentation, biochemical testsmeasuring plasma and urinary metanephrines, 24-hour urine tests for catecholamines andVanillylmandelic Acid (VMA), blood catecholamine tests, genetic counselling for hereditarysyndromes,andimagingmethodssuchasultrasonography,CTscans,MRI,andPET/CTscans. [1,4]

CT scans are often considered the gold standard for diagnosing pheochromocytoma due to theirhigh accuracy in detecting tumours, although PET/CT scans are preferred for detecting bothpheochromocytomasandparagangliomas.[4,5]

Case

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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 bloodpressure was recorded as 210/110. Investigation revealed a suspicion of pheochromocytoma. A CTscan of the abdomen showed a left adrenal tumor measuring 10x10 cm, spherical in shape, with asmooth regular margin and central necrosis, confirming the diagnosis of pheochromocytoma of theleft adrenal gland. Biochemical analysis revealed elevated levels of plasma catecholamines, 24-hourinarycatecholamines, andvanillylmandelic acid(VMA)abovenormal values.

Preoperatively, symptoms of hypertension were managed with oral Alpha-blockers initiated 14-15days before surgery, along with control of tachycardia achieved through βeta-blockers and calciumchannel blockers. The patient's blood pressure was controlled at 120/80, and her heart rate wasmaintainedbetween60-80beats perminute.

Operativemanagementwascarriedoutcollaborativelybyanaesthesiologistsandsurgeons. 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 musclerelaxants were administered for intubation. During intubation and surgery, hypertensive crises werepromptlymanagedwithintravenousnitroprusside,andarrhythmiaswerecontrolledwithlidocaine.

An open surgical approach with a midline incision allowed complete exposure and inspectionof the left adrenal gland. The adrenal vein was identified and clipped, and remaining soft tissueattachments were divided, leading to successful total left adrenalectomy. The patient'spostoperative course was uneventful, with monitoring of blood pressure, volume status, and bloodsugar for the first 24 hours. Postoperatively, blood pressure remained controlled, and the patientwas discharged on the 10th postoperative day. After 5-year follow-up, the patient remained healthywith norecurrence.

On gross examination, the tumor appeared spherical with regular margins and weighed 200grams. Histopathological analysis confirmed the presence of benign pheochromocytomas containingsmallnestsof chromaffincells witheosinophiliccytoplasm.**(Fig1-.8)**

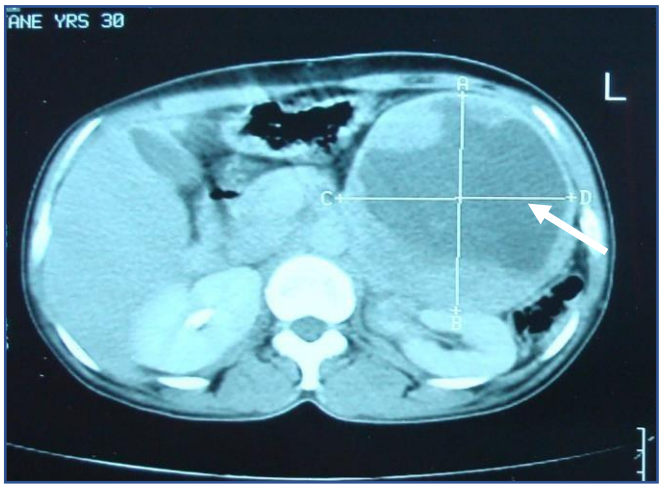

Fig-1 CT abdomen showed a 10x10 cm cystic lesiononleftsideabovethekidney,Apheochromocyto ma

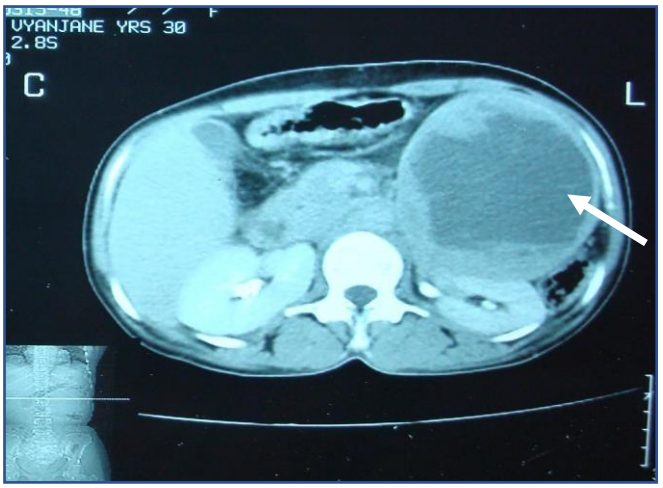

Fig-2 CT abdomen showed a spherical, regularmargintumorwithcentralnecrosis

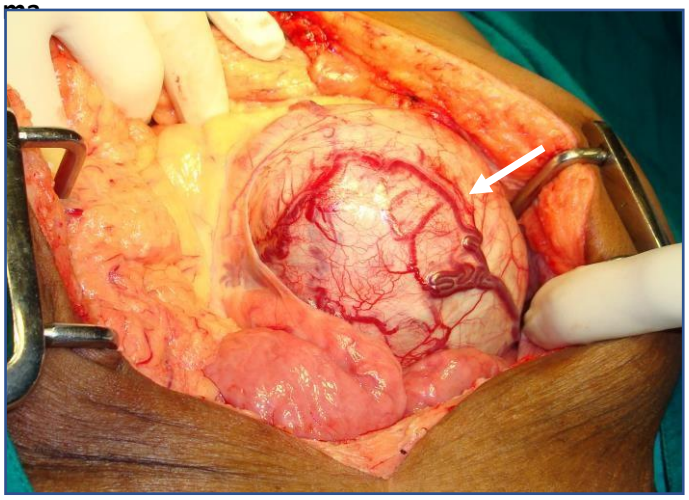

Fig-3 Intra operative photographs a big cystic lesionabovetheleftkidney

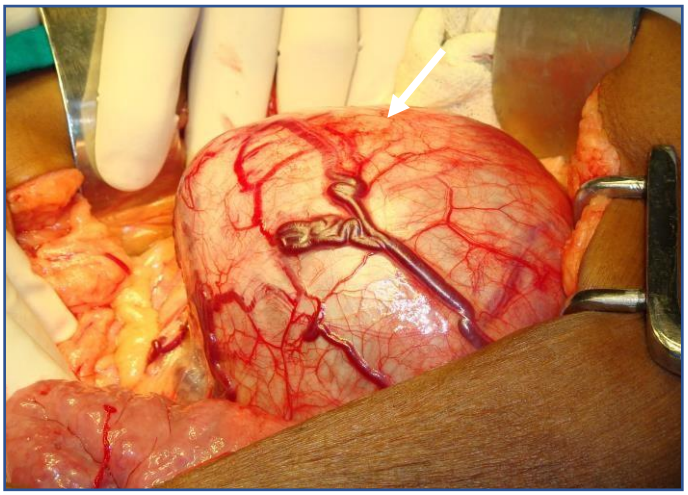

Fig-4 Intra operative photographs a big cystic lesionabovetheleftkidney

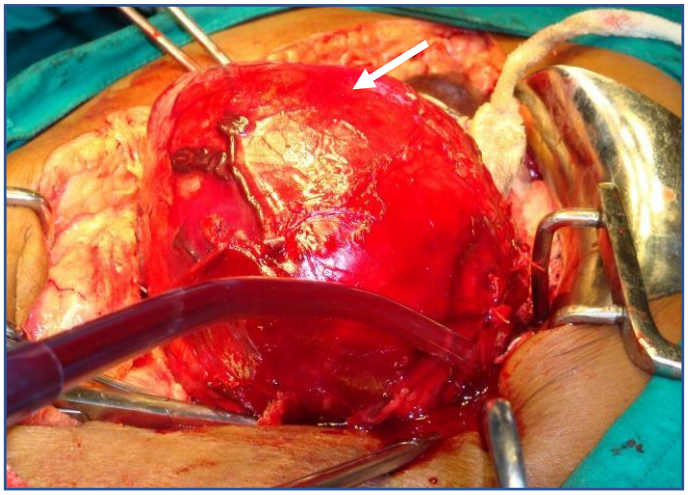

Fig-5 Intra operative photographs showing resectionofleftadrenal tumor

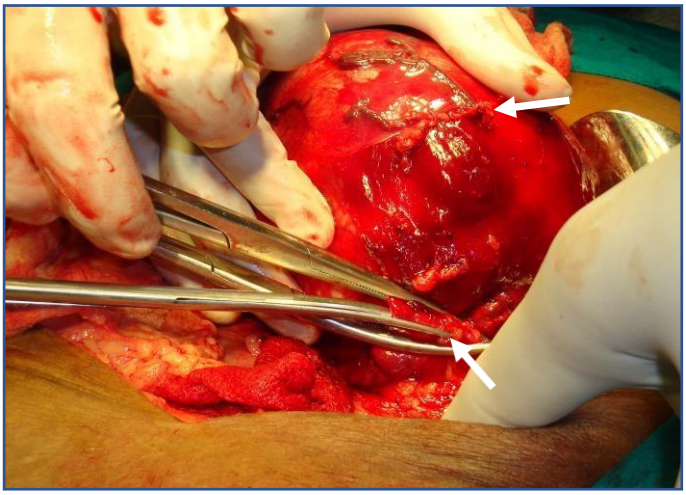

Fig-6 Intra operative photographs showing leftadrenalveinligation."veinfirsttechnique"

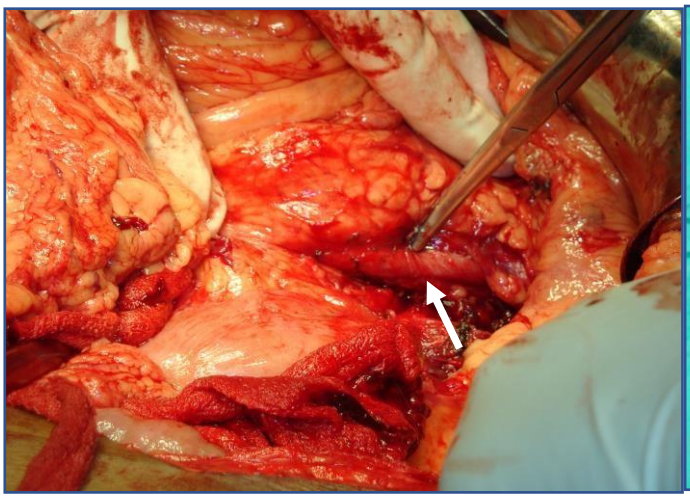

Fig-7 Intra operative photographs showing aorta withtotal leftadrenalectomy.

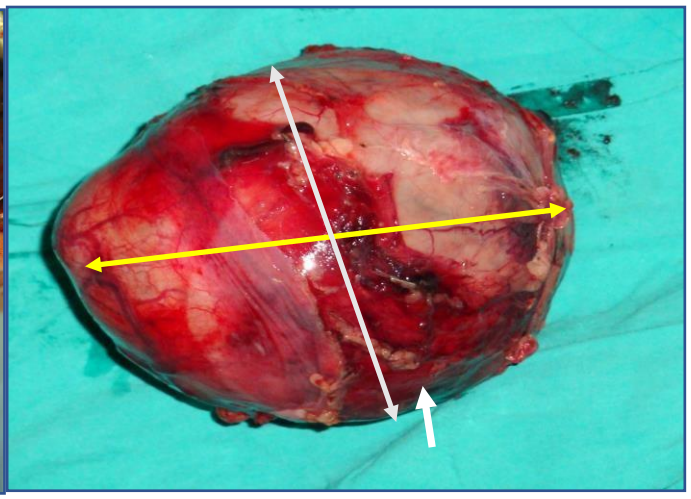

Fig-8 Gross specimen measuring 10x10 cmbenignpheochromocytoma

CaseII

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

Preoperative management involved initiating Alpha-blocker therapy 15 days before surgery tocontrol blood pressure. Beta-blockers were added three days prior to surgery to managetachycardia. Intravascular volume expansion was achieved with the infusion of 1 litter of crystalloidsolution.

Laparoscopicsurgerywasplannedandsurgicaltechniqueinvolvedplacingthepatientinalateral 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 subxiphoidposition for liver retraction. A diagnostic laparoscopy was initially performed to rule out malignancy.Therighthepaticlobewasmobilizedcompletelytofacilitatevisualizationandsafeaccesstothevena cava and adrenal vein. The right adrenal vein was exposed and safely clipped after developing aplane between the vena cava and the medial margin of the adrenal gland. The adrenal gland wasdissectedaway fromtheretroperitoneumonboth sides.

Utilizing the "vein first technique," the main adrenal vein was identified, dissected, and dividedbetween clips. Harmonic bipolar forceps were used for adrenal gland dissection, followed by totaladrenalectomy. A surgical specimen measuring 5x3 cm and oval in shape was extracted through amini-laparotomy site, and a drainage tube was placed for 2 days. Postoperatively, the patient'srecovery was uneventful, and blood pressure remains controlled. The patient was discharged on the5th postoperative day without complications. Histopathological examination confirmed the presenceof a benign pheochromocytoma. After 3-year follow-up, the patient's condition healthy, withoutrecurrence.**(Fig 7-14)**

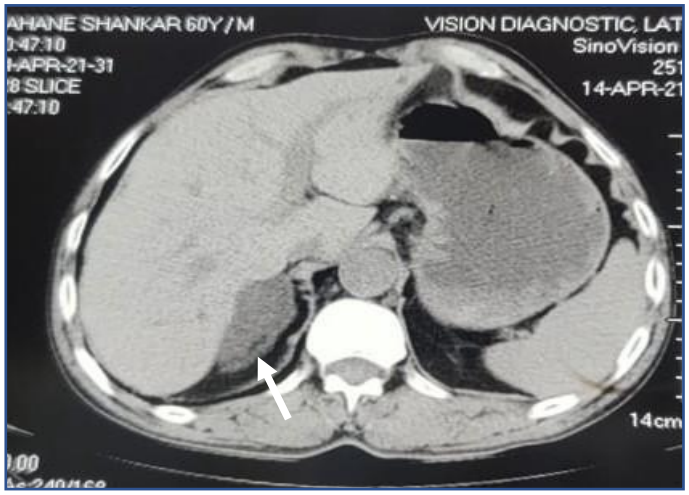

Fig-7CT abdomen showed a 5x3 cm SOL lesion onrightside,abovethekidney,Apheochromocytoma

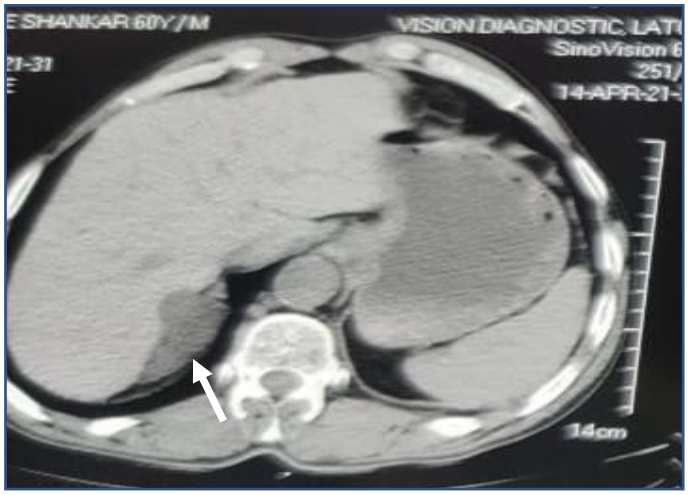

Fig-8CT abdomen showed a 5x3 cm SOL lesion onrightside,abovethekidney,Apheochromocytoma

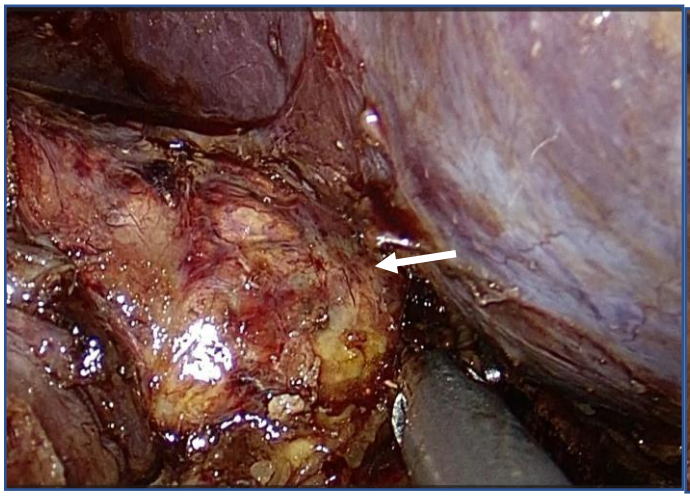

Fig-9Intra operative Laparoscopic photographsshowingrightsideadrenaltumor

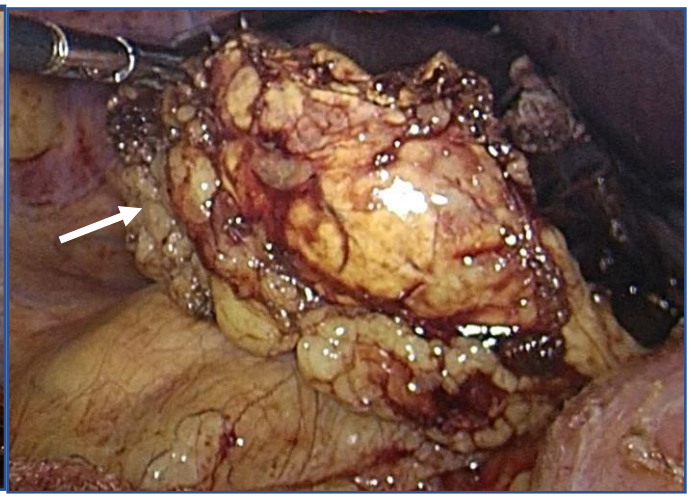

Fig-10 Intra operative Laparoscopic photographsshowingrightsideadrenaltumorofsize5x3cm

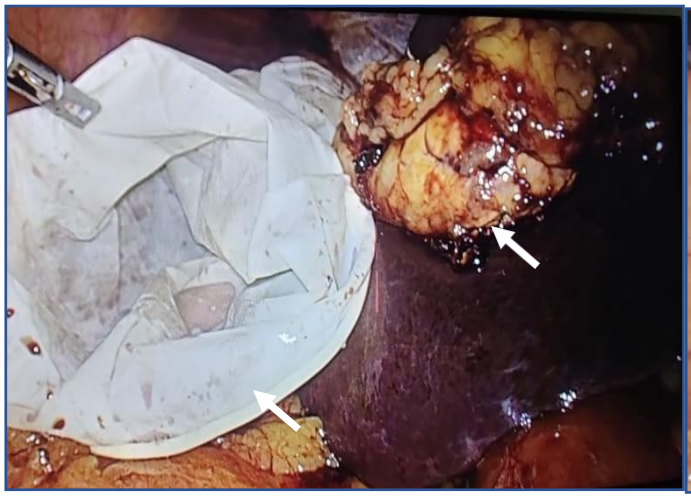

Fig-11 Intra operative Laparoscopic photographsshowingtotalexcisionofsizerightadrenaltumor

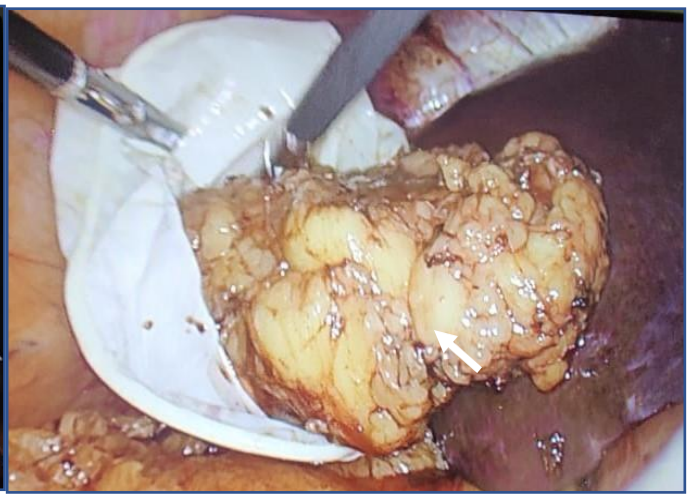

Fig-12IntraoperativeLaparoscopicphotographsshowing right side adrenal tumor with extractionbag

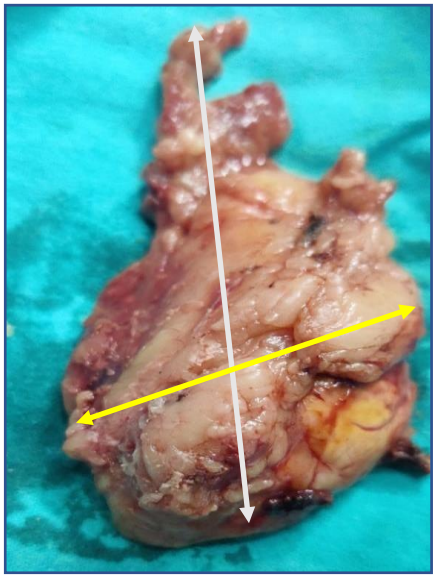

Fig-13Grossspecimenmeasuring5x3cmrightpheochromocytoma

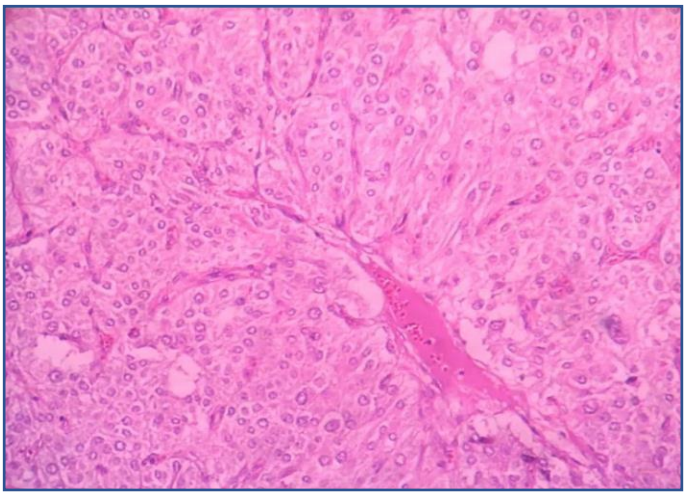

Fig-14 Histopathology showingPheochromocytomatumorwithchromaffincells

Discussion

ProfessorLudwigPick,aGermanphysician,firstcoinedtheterm"pheochromocytoma"in1912. Pheochromocytoma, a benign tumor of the adrenal medulla secreting catecholamines in 90% ofcases, manifests with symptoms such as headache, palpitations, swelling, and hypertension inapproximately 90% of patients. The gold standard imaging modality for identifying adrenalpheochromocytomasis CTabdomen, whichidentifies95%ofthese tumors. [1,2,4,]

Surgical management of pheochromocytoma requires a multidisciplinary team comprisingendocrinologists,surgeons,and anaesthesiologistsexperienced inmanagingthecondition.
Preoperative goals include optimizing blood pressure and normalizing intravascular volume.Adequate preoperative blood pressure control targets a systolic/diastolic blood pressure of 120/80mmHg and a heart rate of 60-80 beats per minute. Patients are encouraged to maintain hydrationwitha high-sodiumdiet beforesurgery.[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 pressurecontrol minimizes hypertensive crises during surgery, reduces adverse effects of anesthesia, andmaintainsstablebloodpressureintraoperatively.[1,2,3]

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

Intraoperative hypertensive crises are managed with intravenous nitroprusside, phentolamine, ornitro-glycerine, while arrhythmias are controlled with esmolol or lidocaine. Adequate volumereplacement is essential to prevent postoperative hypertension, and calcium channel blockers maybe used as primary therapyfor bloodpressurecontrol.[2,3]

Surgical management options for pheochromocytoma include open adrenalectomy andlaparoscopic adrenalectomy. Open surgery is preferred for large tumors (>6-12 cm), tumors indifficult-to-access locations, or suspected malignancy. Laparoscopic adrenalectomy, introduced in1996 by Ganger et al, offers shorter hospital stays and minimal operative morbidity and mortality,makingitsafeandeffective formanagingpheochromocytomairrespectiveoftumorsize.[4,6,9]

Postoperative management involves close observation in the surgical ICU, with management ofhypotension and hypertension as needed. Hourly blood sugar monitoring and prompt treatment ofhypoglycemia are essential, while long-term survival rates following surgical removal of benignpheochromocytomasarehigh,withmostpatientsbecomingnormotensivepostoperatively.[2,3,10]

Conclusion

Pheochromocytoma, a rare tumor secreting catecholamines in 90% of cases, typically requirescomplete surgical removal as the definitive treatment. The gold standard for diagnosingpheochromocytoma involves using CT abdomen imaging and measuring elevated plasma freemetanephrines throughbiochemicaltesting.In cases of benign pheochromocytoma, the preferred approach is minimally invasivelaparoscopic or robotic adrenalectomy. However, for larger tumors exceeding 6-12 cm or those ofbenignormalignant nature, opensurgeryremains thegoldstandardprocedure.Given the complexities involved, effective pheochromocytoma management necessitates theexpertise of an endocrinologist, surgeon, and anaesthesiologists. Thus, a multidisciplinary team isessentialtoensurethesafetyandsuccessof pheochromocytoma surgery.

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