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PHEOCHROMOCYTOMA PRESENTING WITH PAROXYSMAL HYPERTENSION AND ADRENERGIC SYMPTOMS

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Abstract

Background: Pheochromocytoma is a rare catecholamine-secreting tumor of chromaffin cells that classically manifests with episodic headache, palpitations, and sweating, often alongside paroxysmal or sustained hypertension. Delayed recognition exposes patients to preventable cardiovascular complications.

Case: We report an anonymized adult patient who presented with paroxysmal hypertension, adrenergic symptoms, and weight loss. Biochemical evaluation revealed markedly elevated plasma free metanephrines and 24-hour urinary fractionated metanephrines. Cross-sectional imaging demonstrated a unilateral adrenal mass with avid uptake on ^123I-MIBG scintigraphy. Following meticulous preoperative alpha-adrenergic blockade and volume expansion, the patient underwent laparoscopic adrenalectomy. Histopathology confirmed pheochromocytoma with negative margins and a low PASS score. Postoperatively, blood pressure normalized without antihypertensives, and biochemical markers returned to reference ranges.

Conclusion: This case underscores the importance of high clinical suspicion, standardized biochemical testing, targeted imaging, and rigorous preoperative preparation. Early surgical management can be curative and prevents catastrophic cardiovascular events. Long-term follow-up is essential due to the risk of recurrence and the not-infrequent association with hereditary syndromes.

Keywords: Pheochromocytoma; Paraganglioma; Secondary hypertension; Metanephrines; Adrenalectomy;

INTRODUCTION

Pheochromocytomas are catecholamine-producing tumors arising from adrenal medullary chromaffin cells, while extra-adrenal counterparts are termed paragangliomas (collectively PPGL). Although rare, with an estimated incidence of 2–8 per million per year, PPGL represent a clinically significant and potentially curable cause of secondary hypertension, accounting for approximately 0.2–0.6% of hypertensive patients [1–3]. The classical triad—episodic headache, palpitations, and diaphoresis—occurs in only a subset of patients, and presentations range from asymptomatic adrenal incidentalomas to hypertensive crises, cardiomyopathy, or hyperglycemia [1,4,5].

The diagnostic approach hinges on high-sensitivity biochemical assays of catecholamine metabolites—plasma free or urinary fractionated metanephrines—followed by anatomic imaging (CT/MRI) and, when indicated, functional imaging such as ^123I-metaiodobenzylguanidine (MIBG) scintigraphy or positron emission tomography (PET) using ^18F-FDG or ^18F-DOPA, especially in metastatic, recurrent, or hereditary disease [1,6–8]. Surgical excision remains the definitive treatment; minimally invasive adrenalectomy is preferred for localized adrenal tumors, with open approaches reserved for large or invasive lesions [2,9]. Preoperative alpha-adrenergic blockade and judicious volume expansion are critical to mitigate intraoperative hemodynamic instability [10–12].

Genetic predisposition is increasingly recognized; up to 30–40% of patients harbor germline mutations (e.g., RET, VHL, NF1, SDHx, MAX, TMEM127) [2,13–15]. Consequently, many guidelines recommend genetic testing for most patients with PPGL, particularly those with early onset, bilateral tumors, extra-adrenal disease, or a family history [1,2,14]. Postoperative follow-up involves periodic biochemical surveillance and risk-adapted imaging given the potential for recurrence, which may occur years after apparently curative resection [3,16].

Here we present a case of biochemically and radiologically confirmed pheochromocytoma managed with laparoscopic adrenalectomy after standardized preoperative preparation. We discuss diagnostic nuances, perioperative strategies, and follow-up in light of contemporary evidence.

Case Presentation:

An anonymized adult patient in the fourth decade of life presented to the outpatient clinic with a 10-month history of intermittent episodes of pounding headache, palpitations, and profuse sweating. Episodes lasted 15–45 minutes, occurring several times per week, and were frequently accompanied by tremulousness, a sense of impending doom, and labile blood pressure readings captured on a home monitor. The patient reported unintentional weight loss of approximately 6 kg over six months and described episodic facial flushing and exertional dyspnea. There was no history of obstructive sleep apnea, chronic kidney disease, or endocrine disorders. Medications included an as-needed short-acting calcium channel blocker started by a local practitioner; there was no use of tricyclic antidepressants, monoamine oxidase inhibitors, or sympathomimetics. There was no family history of endocrine tumors or early-onset hypertension.

On examination between episodes, the blood pressure was 132/82 mmHg with a heart rate of 84 beats per minute, BMI 25.8 kg/m², and unremarkable cardiovascular, respiratory, and abdominal findings. During a witnessed paroxysm in the clinic, blood pressure surged to 198/106 mmHg with sinus tachycardia at 126 beats per minute and diaphoresis; the episode resolved spontaneously within 30 minutes. There were no cutaneous neurofibromas or mucosal neuromas, and the thyroid examination was normal.

Routine laboratory testing showed fasting plasma glucose of 104 mg/dL and HbA1c 5.7%. Renal and liver function tests were within reference ranges; TSH was normal. Given the symptom constellation and paroxysmal hypertension, biochemical testing for catecholamine excess was performed. Supine plasma free metanephrines were markedly elevated: metanephrine 1.92 nmol/L (reference <0.50) and normetanephrine 4.68 nmol/L (reference <0.90). A confirmatory 24-hour urinary fractionated metanephrine profile demonstrated metanephrine 1,850 µg/24 h (reference <350) and normetanephrine 6,200 µg/24 h (reference <600), with adequate creatinine correction. Interfering medications and stressors were reviewed and deemed unlikely contributors [1,6].

Contrast-enhanced CT of the abdomen revealed a 4.2 × 3.8 cm well-circumscribed, heterogeneously enhancing mass in the right adrenal gland, with no macroscopic fat and washout characteristics atypical for a benign adenoma. There was no local invasion or lymphadenopathy. MRI confirmed a hyperintense lesion on T2-weighted images ("light-bulb bright" appearance) with restricted diffusion, consistent with pheochromocytoma [7,8]. Functional imaging with ^123I-MIBG showed avid tracer uptake confined to the right adrenal lesion, without extra-adrenal foci or metastases. (Fig 1 & 2). Echocardiography demonstrated preserved left ventricular ejection fraction (60%) without wall motion abnormalities; there was no evidence of catecholamine-induced cardiomyopathy.

The patient underwent standardized preoperative optimization. Oral phenoxybenzamine was initiated at 10 mg twice daily and titrated to 20 mg thrice daily over 10 days to achieve target seated blood pressures of 120–130/80–85 mmHg with mild orthostatic hypotension (standing systolic drop 10–15 mmHg) and resolution of paroxysms [10,11]. Liberal salt intake and volume expansion were encouraged. After alpha blockade was established, a cardioselective beta-blocker (metoprolol 25 mg twice daily) was added to control tachycardia. Preoperative hematocrit rose from 37% to 41%, consistent with volume repletion.

The patient underwent elective transperitoneal laparoscopic right adrenalectomy under general anesthesia with invasive arterial monitoring and central venous access. An experienced anesthesia team implemented a pheochromocytoma protocol: gentle induction, avoidance of agents that provoke catecholamine release, and readiness with short-acting vasodilators (sodium nitroprusside) and vasopressors (phenylephrine, vasopressin) [12].

Intraoperative hemodynamic instability was limited to transient hypertensive surges during tumor manipulation, effectively managed with titrated vasodilators; hypotension after adrenal vein ligation responded to fluids and vasopressors. Estimated blood loss was 70 mL, operative time 120 minutes, and there were no complications.

Postoperatively, the patient was monitored in a high-dependency unit for 24 hours. Antihypertensives were withheld. Blood pressure stabilized at 116–124/72–78 mmHg with heart rates of 68–82 beats per minute. Plasma glucose remained normal. The patient was discharged on postoperative day 3.

Histopathology confirmed pheochromocytoma with classic Zellballen architecture, positive chromogranin A and synaptophysin immunostaining, S-100 positive sustentacular cells, and a PASS (Pheochromocytoma of the Adrenal gland Scaled Score) of 2, indicating a low risk of aggressive behavior. Margins were negative. At 6-week follow-up, symptoms had resolved completely. Plasma free metanephrines normalized (metanephrine 0.22 nmol/L, normetanephrine 0.41 nmol/L). At 12 months, the patient remained normotensive without medication and had no biochemical or imaging evidence of recurrence.

With pre- and postoperative counseling, the patient consented to genetic evaluation. A multigene panel was discussed; given the sporadic presentation, unilateral tumor, and absence of suggestive stigmata, the patient elected deferred testing after shared decision-making. The follow-up plan included annual metanephrine testing and risk-adapted imaging, with earlier evaluation for recurrent symptoms [1–3,16].

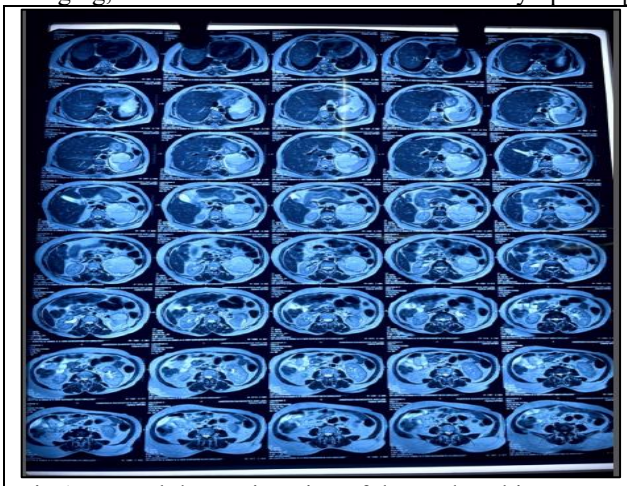

Fig 1- MRI abdomen imaging of the study subject

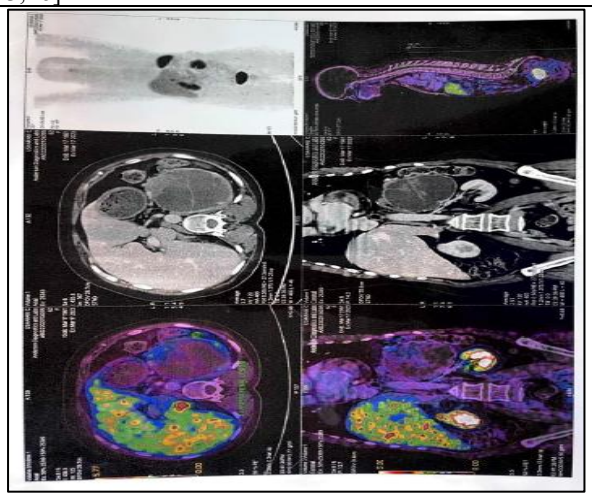

Fig 2- CECT-abdomen imaging of the study subject

Differential Diagnosis

The differential diagnosis for paroxysmal hypertension and adrenergic symptoms includes hyperthyroidism, panic disorder, medication- or substance-induced sympathetic activation (e.g., amphetamines, decongestants), obstructive sleep apnea, hypoglycemia, autonomic epilepsy, and baroreflex failure [1,4,5]. For an adrenal mass, differentials include lipid-poor adenoma, adrenocortical carcinoma, metastasis, and rare vascular lesions. The markedly elevated metanephrines and characteristic imaging favored pheochromocytoma over these alternatives.

Management and Outcome

Management centered on (1) biochemical confirmation of catecholamine excess, (2) precise localization with CT/MRI and functional imaging, (3) rigorous preoperative alpha blockade and volume expansion, and (4) minimally invasive adrenalectomy by an experienced team, followed by surveillance. The favorable postoperative course—rapid symptom resolution, withdrawal of antihypertensives, normalization of metanephrines, and reassuring histopathology—supports a curative resection. Long-term follow-up is planned because late recurrences can occur even after apparently complete excision [3,16].

DISCUSSION

This case illustrates the prototypical yet often under-recognized presentation of pheochromocytoma. Several points merit emphasis: optimal biochemical testing, imaging strategy, perioperative preparation, surgical approach, and follow-up including genetic considerations.

Biochemical diagnosis: Measurement of plasma free metanephrines or 24-hour urinary fractionated metanephrines is recommended as first-line testing due to high sensitivity (often >95%) stemming from continuous intratumoral conversion of catecholamines to metanephrines [1,6]. Plasma assays should be performed with the patient in a supine position after rest to reduce false positives [1]. Marked elevations (>3–4× upper reference limit), as in this patient, have a high positive predictive value and generally obviate the need for confirmatory suppression tests [1,6]. Borderline results warrant careful review of confounders (stress, acute illness, OSA, caffeine, nicotine) and medications (TCAs, SNRIs, levodopa), and in equivocal cases, clonidine suppression testing may be helpful [1,6]. Our patient's robust biochemical excess and compatible imaging simplified the pathway to surgery.

Imaging: CT provides excellent spatial resolution and is widely available; MRI is preferred when radiation or contrast exposure is undesirable and is particularly useful for extra-adrenal paragangliomas with its characteristic T2 hyperintensity [7,8]. Functional imaging adds specificity and assists in staging, particularly in suspected multifocal or metastatic disease and in hereditary syndromes [7,8]. MIBG scintigraphy is highly specific for adrenergic tissue, whereas ^18F-FDG or ^68Ga-DOTATATE PET/CT may be superior in certain genotypes (e.g., SDHB) and

aggressive disease [7,8,14]. In this case, CT/MRI localized a 4.2 cm adrenal mass and MIBG confirmed catecholamine avidity without metastases, supporting a minimally invasive approach.

Preoperative preparation: Optimal alpha blockade is the cornerstone of safe resection. Phenoxybenzamine, a nonselective, noncompetitive alpha antagonist, remains widely used; selective alpha-1 blockers (doxazosin, prazosin) are alternatives with fewer side effects but possibly more intraoperative lability in some series [10,11]. Targets include controlled seated blood pressure with mild orthostasis, heart rate <80–90 beats per minute, and evidence of volume repletion (rise in hematocrit, reduced orthostatic symptoms) [10,11]. Salt loading and liberal fluids are recommended. Beta blockade should never precede alpha blockade to avoid unopposed alpha-adrenergic vasoconstriction [10–12]. Calcium channel blockers can be adjuncts, particularly for residual hypertension or when alpha blockers are not tolerated [10]. Case series and guidelines consistently link structured preparation to reduced perioperative cardiovascular complications [10–12].

Anesthetic and intraoperative management: Hemodynamic volatility during induction and tumor manipulation necessitates vigilant monitoring and readily titratable vasoactive agents [12]. Short-acting vasodilators (nitroprusside, nicardipine) are effective for hypertensive surges; volume resuscitation and vasopressors manage post-ligation hypotension. Avoiding drugs that release histamine or provoke sympathetic discharge is prudent. Our patient experienced predictable but manageable fluctuations, reflecting successful preparation and intraoperative coordination.

Surgical approach: Laparoscopic adrenalectomy is standard for unilateral, localized pheochromocytomas typically ≤6 cm without radiological invasion [2,9]. It offers reduced pain, shorter hospitalization, and faster recovery relative to open surgery [2,9]. Open adrenalectomy is reserved for large (>6–8 cm), invasive, or malignant tumors requiring en bloc resection [2]. Tumor handling should minimize catecholamine release. In experienced hands, conversion rates and complications are low; our patient's uneventful course mirrors contemporary outcomes [2,9].

Pathology and risk assessment: Classic histology shows Zellballen nests of chief cells with sustentacular S-100 positive cells; immunoreactivity for chromogranin A and synaptophysin supports neuroendocrine lineage. No single histologic system reliably predicts malignant behavior; PASS and GAPP scores provide risk stratification but are imperfect [9,17]. Malignancy is defined by the presence of metastases in non-chromaffin sites (e.g., bone, lung, liver) rather than histologic features alone [9]. The low PASS in this case supports a low risk of aggressive behavior, but long-term surveillance remains essential.

Genetics: Up to 30–40% of PPGL arise in the setting of germline pathogenic variants [2,13–15]. Genotype informs tumor location, biochemistry, imaging choice, and metastatic risk; for instance, SDHB mutations confer higher metastatic potential and greater ^18F-FDG avidity [14,15]. Many guidelines advocate offering genetic testing broadly, particularly to patients with early onset, bilateral disease, extra-adrenal tumors, or a family history [1,2,14].

Although our patient elected to defer testing after counseling, documentation of informed decision-making and re-discussion at follow-up are important because the result may influence surveillance intensity and cascade testing in relatives.

Cardiometabolic manifestations: Catecholamine excess can precipitate labile hypertension, arrhythmias, stress (Takotsubo-like) cardiomyopathy, glucose intolerance, and weight loss [4,5,18]. In reported cases, myocardial stunning and reversible cardiomyopathy often improve after tumor removal [18]. Our patient had no echocardiographic impairment, but preoperative screening was valuable to stratify risk.

Long-term follow-up: Biochemical testing (plasma or urine metanephrines) at 2–6 weeks postoperatively confirms biochemical cure; subsequent annual surveillance is commonly recommended for at least 10 years, and lifelong in high-risk patients (young age, hereditary syndromes, large tumors, paragangliomas) [3,16]. Recurrences may occur late; therefore, patient education regarding symptom vigilance is crucial. Our follow-up plan aligns with endocrine society and European recommendations [1–3,16].

Comparison with literature: Numerous case reports and series echo key themes from this case. Typical presentations include paroxysmal adrenergic symptoms and hypertension, with some patients misdiagnosed as anxiety or panic disorder [4,5]. Biochemical confirmation with metanephrines consistently outperforms direct catecholamine assays in sensitivity [1,6]. Imaging combinations (CT/MRI plus MIBG or PET) enhance localization and staging, particularly in hereditary contexts [7,8,14]. Across cohorts, structured alpha blockade reduces intraoperative crises and postoperative complications [10–12]. Laparoscopic adrenalectomy has become the predominant approach for suitable adrenal lesions, with low morbidity and rapid recovery [2,9]. Histopathologic scoring systems aid risk discussion but do not replace clinical and genetic risk markers [9,17]. Finally, long-term biochemical surveillance is universally endorsed given non-trivial recurrence rates even beyond five years [3,16].

In summary, the present case exemplifies evidence-based practice: high clinical suspicion, appropriate biochemistry performed under optimal conditions, targeted multimodality imaging, disciplined preoperative preparation, minimally

invasive surgery by a specialized team, and commitment to long-term follow-up with shared decision-making about genetic testing.

Patient Perspective (optional)

The patient reported that the most troubling aspects before diagnosis were unpredictable episodes of palpitations and anxiety-like symptoms that interfered with social activities and work. After surgery, the patient expressed relief at the resolution of attacks and the ability to discontinue antihypertensive medication. The patient appreciated preoperative counseling that explained medication sequencing and intraoperative risks.

CONCLUSION

Pheochromocytoma, while rare, should be considered in patients with paroxysmal hypertension and adrenergic symptoms. Diagnostic confirmation with plasma free or urinary fractionated metanephrines followed by focused cross-sectional and functional imaging enables curative surgical planning. Intensive preoperative alpha blockade, careful anesthetic management, and minimally invasive adrenalectomy are central to safe outcomes. Given the substantial proportion of hereditary cases and the potential for late recurrence, individualized genetic counseling and long-term biochemical surveillance are indispensable components of care [1–3,14,16].

Declarations

Patient consent: Written informed consent for anonymized publication of clinical details and images was obtained.

Conflicts of interest: None declared.

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