Clinical, Imaging, and Biochemical Presentation of Cystic Pheochromocytomas

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SUMMARY:

Objective: Cystic adrenal mass is a rare imaging presentation of pheochromocytoma. We aimed to describe the clinical, biochemical, and imaging characteristics of patients with cystic pheochromocytoma.

Design: Single-center, retrospective study, 2000–2020.

Patients: Consecutive patients with cystic pheochromocytoma identified from our institutional pathology and adrenal tumor database.

Results: Of the 638 patients with pheochromocytomas, 21 (3.2%) had cystic pheochromocytomas (median age 57 years, 57% women). Most pheochromocytomas were discovered incidentally (57%) or due to symptoms of catecholamine excess (24%). The median tumor size was 6.4 cm. On imaging, cystic pheochromocytomas were round or oval (90%), heterogeneous lesions (86%) with a thick solid rim (median rim thickness 13.9 mm, unenhanced CT attenuation 40 HU, venous-phase CT attenuation 83 HU), and a median cystic component of 40% (unenhanced CT attenuation 17.6 HU, venous-phase CT attenuation 20.4 HU), and rarely with calcifications (15%). All 20 patients with biochemical testing had functioning tumors (adrenergic in 80%, noradrenergic in 20%). Total urinary metanephrine excretion correlated with the volume of the solid component (R2=0.75, *P*<0.0001) but not the cystic component (R2=0.04, *P*=0.4386). All patients underwent adrenalectomy (48% laparoscopic, 52% open), and the median duration of hospital stay was 4 days.

Conclusion: Cystic pheochromocytomas are rare, large tumors with a phenotypic appearance that can masquerade as other adrenal cystic lesions. The degree of biochemical abnormality in cystic pheochromocytomas is associated with the volume of the solid component. All patients with adrenal cysts that have a solid component or an unenhanced attenuation >10 HU should undergo biochemical testing for pheochromocytoma.

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Keywords

adrenalectomy; metanephrine; Hounsfield unit; solid component; cystic component

INTRODUCTION

Pheochromocytomas are rare catecholamine-secreting neuroendocrine tumors arising from the chromaffin cells in the adrenal medulla. In a population-based study of 1287 patients with adrenal tumors, pheochromocytomas represented 1.1%[1]. Most pheochromocytomas are discovered incidentally on imaging performed for reasons other than adrenal mass[2] and are typically solid tumors with unenhanced attenuation on computed tomography (CT) of > 20 Hounsfield units (HU)[3,4]. While presence of focal cystic changes in pheochromocytomas are common[5], presentation with a macroscopic cystic component is rare. These cases may pose a diagnostic challenge risking inadequate preparation for surgery due to misdiagnosis as an adrenal cyst. Due to its rarity, evidence regarding cystic pheochromocytomas is limited to case reports or small pathology-based series of up to six patients [6–10].

Accurate preoperative diagnosis of pheochromocytoma is important to assure the best perioperative outcomes. Our objectives were to (1) characterize the clinical, biochemical, imaging characteristics and outcomes of patients with cystic pheochromocytoma and (2) determine the association of the solid and cystic component volumes of pheochromocytoma with the degree of catecholamine excess.

METHODS

Patient selection

The study protocol was approved by our Institutional Review Board. Patients were included if 1) they were evaluated at our institution between January 1st, 2000 and December 31st, 2020; 2) histopathology was available and reported a cystic element; and 3) imaging (CT or magnetic resonance imaging [MRI]) demonstrated that   10% of pheochromocytoma volume was cystic. We first interrogated our longitudinal adrenal database on July 1st, 2021 to identify all patients with pheochromocytoma during the study period (n=638). We also interrogated the institutional pathology database of all pathology reports resulting from adrenalectomy using the terms "cyst" or "cystic" combined with term "pheochromocytoma" (n=87). Final cohort of patients meeting eligibility criteria (n=21) was reached after combining the search results from the two databases, and a detailed review of imaging and pathology reports.

Data collection

Information on clinical presentation, genetic testing, biochemical parameters, imaging phenotype, and management was collected. Biochemical parameters included plasma fractionated metanephrine (normal <0.5 nmol/L) and normetanephrine (normal <0.9 nmol/L), 24-hour urinary fractionated metanephrine (normal <2028 nmol/day) and normetanephrine (normal <4913 nmol/day), and 24-hour urinary fractionated catecholamines (epinephrine [normal <115 nmol/day], norepinephrine [normal <473

nmol/day], dopamine [normal <2611 nmol/day]). Pheochromocytoma was classified as 'adrenergic' when both metanephrine and normetanephrine levels were elevated and 'noradrenergic' when only normetanephrine levels were elevated.

All imaging was reviewed by two investigators in duplicate (DP and PN). An abdominal radiologist with 3 years post fellowship experience (PN), calculated the total tumor volume, the volume of the solid and cystic components, unenhanced and contrast enhanced CT attenuation of the solid and cystic components, and rim thickness. At the time of imaging review and measurements, PN was blinded to patients' clinical presentation and outcomes. All images were reviewed on a clinical workstation (EIZO RX360, EIZO inc. Cypress, California, USA) with all segmentation and measurements performed using imaging specific software (Visage Client 7.1.16, Visage imaging, Victoria, Australia)

Statistical analysis

Categorical data were presented as counts and percentages and continuous data were presented as median and interquartile ranges. Simple bivariate analysis was used to assess association between continuous variables. Statistical analysis was performed using JMP software, version 14.

RESULTS

Of 7724 patients with adrenal tumors evaluated at our institution between January 1, 2000, to December 31, 2020, 638 (8.3%) were pheochromocytomas. Cystic pheochromocytomas were diagnosed in 21 patients, representing 3.2% of all patients with pheochromocytomas, and 0.27% of all adrenal tumors.

The median age at presentation in the 21 patients with cystic pheochromocytomas was 57 years (IQR 51–67), and 12 (57%) were women. Mode of discovery was incidental in 12 (57%) patients, symptoms of catecholamine excess in 5 (24%), symptoms of mass effect in 2 (10%), genetic case detection testing in 1 (5%) patient, and 1 patient was not recognized to have pheochromocytoma until after adrenalectomy. Regardless of the mode of discovery, 13 (62%) patients endorsed symptoms and signs of catecholamine excess, with spells, palpitations, and paroxysmal or sustained hypertension being most common (Table 1). Genetic testing was pursued only in 6 (29%) patients and 3 patients had positive results: multiple endocrine neoplasia type 2A (n=1), neurofibromatosis type 1 (n=1), and von-Hippel Lindau disease (n=1). Seven (33%) patients had an active or history of extra-adrenal malignancy, including medullary thyroid cancer in the patient with multiple endocrine neoplasia type 2A and gastric cancer in the patient with neurofibromatosis type 1 (Table 1).

Most patients presented with unilateral pheochromocytoma (15, 71% right, and 4, 19% left). In two patients with bilateral pheochromocytomas, only one was cystic. Cystic pheochromocytomas had a round or oval shape in 19 (90%) patients, and lobulated shape in the 2 (10%) patients. In 18 (86%) patients, cystic pheochromocytomas had heterogeneous appearance with septae present in 15 patients. On preoperative imaging, the median tumor size was 6.4 cm (IQR 5–11.1), and the median tumor volume was 115 cm^3 (IQR 47.4–

654.1). The cystic component of the pheochromocytomas varied widely and represented a median of 40% (IQR 24–60) corresponding to a median volume of 48.7 cm^3 (IQR 15.6–236.3) (Table 2). The solid component of the pheochromocytomas represented a median of 60% (40–76%) corresponding to a volume of 61.2 cm^3 (IQR 27.3–186.2). In 16 patients with unenhanced CT imaging available, the median attenuation was 17.6 HU (IQR 14.6–20) within the cystic component and 40 HU (IQR 32.1–44.3) in the solid component of pheochromocytoma. In the 14 patients with contrast-enhanced CT images available, the median attenuation of the cystic component was 20.35 HU (IQR 14.9–26.8), while in the solid component of pheochromocytoma, it was 93 HU (IQR 83.3–121). Only 3 (15%) patients demonstrated calcifications on CT. All pheochromocytomas were well-circumscribed and had a surrounding rim of variable thickness (median rim thickness of 14 mm [IQR 8–22]) that demonstrated significant rim enhancement on contrast-enhanced CT (Tables 1 and 2) (Figures 1 and 2).

For the 20 patients who had a preoperative evaluation by an endocrinologist, the primary reason for referral was a concern for pheochromocytoma in 12 (60%) and work-up for an adrenal mass in 8 (40%), with all ultimately recognized as pheochromocytoma preoperatively. The preoperative diagnosis in the 1 patient who did not have work-up for catecholamine excess was thought to be an adrenal metastasis from renal cell carcinoma. Plasma-free fractionated metanephrines were abnormal in all 18 patients who were tested with a median value of 2.7 nmol/L (IQR 0.9–8.7) for metanephrine and 13.2 nmol/L (IQR 3.2–23.6) for normetanephrine. Similarly, 24-hr urine testing was abnormal in all 16 patients who were tested with a median metanephrine excretion of 15828 nmol/day (IQR 5663–33731) and median normetanephrine excretion of 22957 nmol/day (IQR 9206–84472) (Table 1). Most patients (11, 55%) had plasma or urine fractionated metanephrines at least 10 times the upper limit range of normal or higher (Table 2). All 20 patients with preoperative work-up for catecholamine excess had functioning pheochromocytomas: 16 (80%) with adrenergic profile and 4 (20%) with noradrenergic profile (Table 1). Concentrations of the total urinary metanephrines were associated with the largest tumor diameter (R2=0.38, P=0.009), total tumor volume (R2=0.5, P=0.0021), and solid component volume (R2=0.75, P<0.0001), but not the cystic component volume of pheochromocytoma (R2=0.04, P=0.4386).

In 20 patients in whom pheochromocytoma was diagnosed before surgery, preoperative alpha-adrenergic blockade (phenoxybenzamine in 16, doxazosin in 4) for a median duration of 15.5 days (IQR 10.3–20) was administered. In addition, 17 (85%) patients were treated with beta-adrenergic blockade. Finally, 4 (20%) patients received metyrosine for a median duration of 5 days (IQR 2.8–8) prior to surgery, per our institutional protocol[11]. All 21 patients underwent adrenalectomy, 10 (47.6%, median tumor size 5.7 cm [IQR 4.3–6.4]) via laparoscopic approach and 11 (52.4%, median tumor size 10.1 cm [IQR 6.8–11.9]) via open laparotomy. The median duration of hospitalization was 4 days (IQR 2–6.5). Other than nausea and pain, the 30-day postoperative complications included hypotension and need for vasopressors in 3 patients, acute hypoxia due to pulmonary edema in 1, postoperative ileus in 1 patient and retroperitoneal hemorrhage in the 1 patient identified post-adrenalectomy. Four patients died between 29 to 91 months after surgery, 3 patients due to complications

related to extra-adrenal malignancy, and one because of metastatic pheochromocytoma. (Table 1)

DISCUSSION

In this largest to date study of patients with cystic pheochromocytomas, we describe the prevalence, clinical presentation, biochemical parameters, imaging characteristics, and approaches to management.

We found that cystic pheochromocytomas are extremely rare and accounted for 3.2% of pheochromocytomas and 0.27% of adrenal tumors evaluated at our center over two decades. Prevalence of cystic pheochromocytoma in our study was similar to the prior study on cystic adrenal neoplasms from our institutional pathology database (1973–1998) [7]. Most cystic pheochromocytomas in our study were found incidentally, while the symptoms of hormone excess led to the discovery of only a quarter of our patients.

Biochemical evaluation with plasma or urinary fractionated metanephrines is a mainstay of preoperative diagnosis of pheochromocytoma. However, biochemically silent pheochromocytomas occur in <5% of cases[2]. In a smaller study that included 6 patients with cystic pheochromocytoma, only 3 patients demonstrated catecholamine excess, suggesting a lower secretory capacity of cystic pheochromocytomas[10]. Our findings are discrepant from this study as all cystic pheochromocytomas in our series were biochemically active, and the majority of patients did report symptoms and signs of catecholamine excess, even when diagnosed incidentally based on imaging. We found the excretion of total urinary metanephrines was associated with the volume of the solid component but not the cystic component. Thus, a near-complete cystic pheochromocytoma could be less biochemically active, potentially explaining the differences to the previous smaller study. The cystic component is likely the result of hemorrhagic degeneration due to the large size and rich vascular supply of pheochromocytomas predisposing these tumors to a high frequency of spontaneous hemorrhage[12].

In our cohort of patients with cystic pheochromocytoma, the peak incidence was during the 6th decade of life with a slight female predominance. We found cystic pheochromocytomas to be round or oval-shaped tumors with well-defined borders and rarely with calcifications. For unclear reasons, these tumors showed a predilection for the right side. The median unenhanced CT attenuation of the cystic component in cystic pheochromocytomas was similar to benign adrenal cysts, and that of the solid component was in the range of non-cystic pheochromocytoma. Unlike benign adrenal cysts, cystic pheochromocytomas were more likely to present as heterogeneous lesions and have a thick rim exhibiting significant enhancement following contrast administration (Figure 2). This thick rim comprises solid hypersecreting chromaffin tissue.

An open surgical approach may be favored over laparoscopic surgery in some patients with cystic pheochromocytoma due to the risk of intraoperative tumor capsule rupture, especially when the pheochromocytoma is large-sized or with a significant eccentric cystic component. Rupture of a pheochromocytoma intraoperatively is a potentially fatal complication due to

hemorrhage and subsequent peritoneal deposits with pheochromocytoma tissue [13]. In our series, nearly half of the patients, with markedly larger than average tumour size, underwent adrenalectomy via an open surgical approach. Most patients had an uneventful postoperative recovery. Vasoplegia following resection requiring ICU care and blood pressure support occurred in 14% of patients.

In comparison to patients with non-cystic pheochromocytomas, patients with cystic pheochromocytomas present with a larger size, and are more likely to undergo open adrenalectomy, however otherwise present with similar clinical symptoms[2] (Table 3).

One of the main strengths of our study is a relatively larger sample size compared to prior studies, enabling an analytical review of clinical, biochemical, and imaging characteristics of cystic pheochromocytomas. We acknowledge several limitations in our study, primarily due to the retrospective design, making biases related to information, imaging, and selection particularly likely. Additionally, the small sample size and this being an experience of a single center may limit the generalizability of our observations and results. However, considering the rarity of cystic pheochromocytoma, a prospective design with an adequate sample size may not be feasible.

In conclusion, cystic pheochromocytoma is a rare phenotypic variant, presenting various imaging appearances that could masquerade as other adrenal lesions. Though certain imaging characteristics such as a thick enhancing rim and heterogeneous parenchyma raise suspicion for a cystic pheochromocytoma, abnormal biochemical testing (plasma or urinary fractionated metanephrines) provides better preoperative diagnostic accuracy. Therefore, all patients with cystic lesions of the adrenal gland, except in those with an unenhanced CT attenuation of < 10 HU or with the typical appearance of a benign adrenal cyst (thin rim, homogenous appearance, no solid component or septae, and lack of intracystic contrast enhancement), should undergo evaluation for catecholamine excess to help with management decisions.

FUNDING STATEMENT:

DATA AVIALABILITY STATEMENT:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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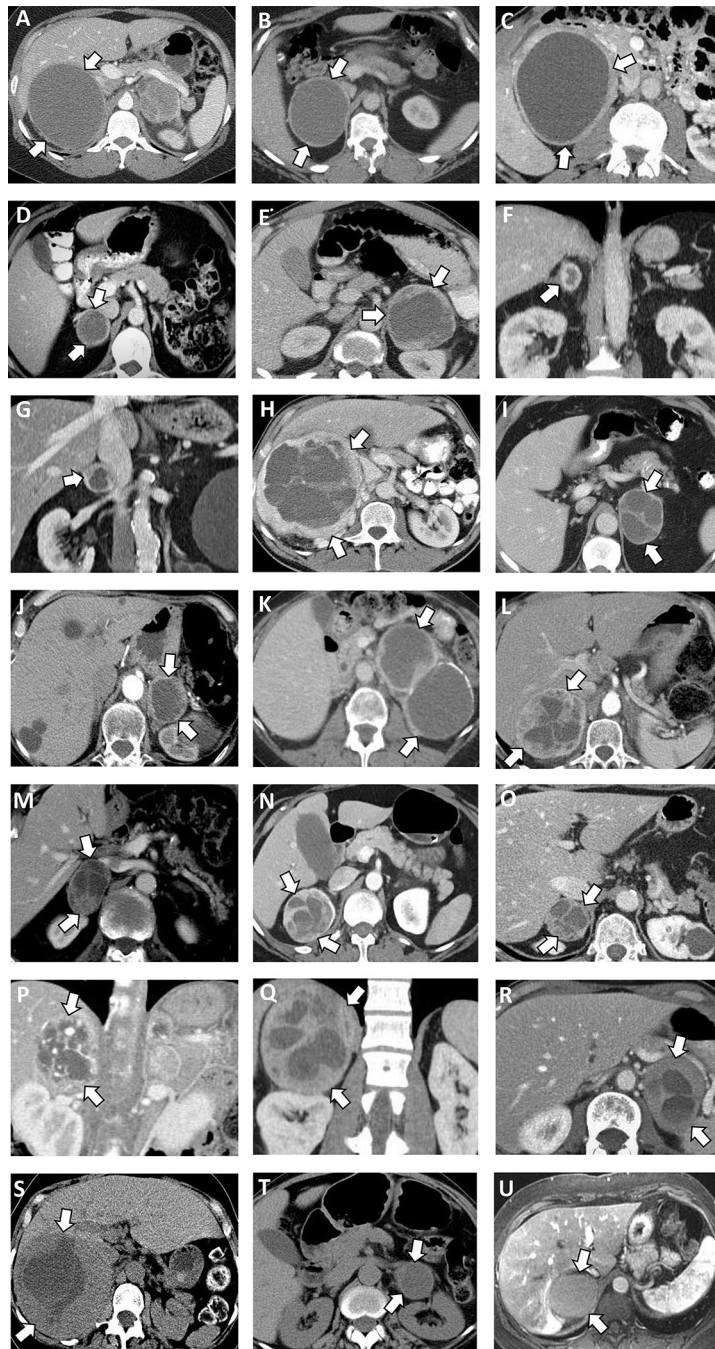
Figure 1. Computed tomography (CT) and magnetic resonance imaging (MRI) imaging of 21 patients with cystic pheochromocytomas.

(A) Right 11.2 cm pheochromocytoma, cystic component 75%, on contrast enhanced CT.

(B) Right 9.1 cm pheochromocytoma, cystic component 77% on contrast enhanced CT.

(C) Right 11.7 cm pheochromocytoma, cystic component 68% on contrast enhanced CT.

(D) Right 4.1 cm pheochromocytoma, cystic component 26% on contrast enhanced CT.

(E) Left 8.2 cm pheochromocytoma, cystic component 50% on contrast enhanced CT.

(F) Left 2.9 cm pheochromocytoma, cystic component 15% on contrast enhanced CT.

(G) Right 3.8 cm pheochromocytoma, cystic component 24% on contrast enhanced CT.

(H) Right 18.9 cm pheochromocytoma, cystic component 40% on contrast enhanced CT.

(I) Left 6.4 cm pheochromocytoma, cystic component 53% on contrast enhanced CT.

(J) Left, 5.0 cm pheochromocytoma, cystic component 50% on contrast enhanced CT.

(K) Left 12.0 cm pheochromocytoma cystic component 64%, peripheral calcification on contrast enhanced CT.

(L) Right 8.2 cm pheochromocytoma, cystic component 28% on contrast enhanced CT.

(M) Right 5.5 cm pheochromocytoma, cystic component 44% on contrast enhanced CT.

(N) Right 6.5 cm pheochromocytoma, cystic component 29% on contrast enhanced CT.

(O) Right 4.4 cm pheochromocytoma, cystic component 24% on contrast enhanced CT.

(P) Right 5.0 cm pheochromocytoma, cystic component 24% on contrast enhanced CT.

(Q) Right 13.5 cm pheochromocytoma, cystic component 23% on contrast enhanced CT.

(R) Left 6.3 cm pheochromocytoma, cystic component 25% on contrast enhanced CT.

(S) Right 14.9 cm pheochromocytoma, cystic component 22% on unenhanced CT.

(T) Left 5.7 cm pheochromocytoma, cystic component 56% on unenhanced CT.

(U) Right 6.3 cm pheochromocytoma, cystic component 70% on contrast enhanced MRI.
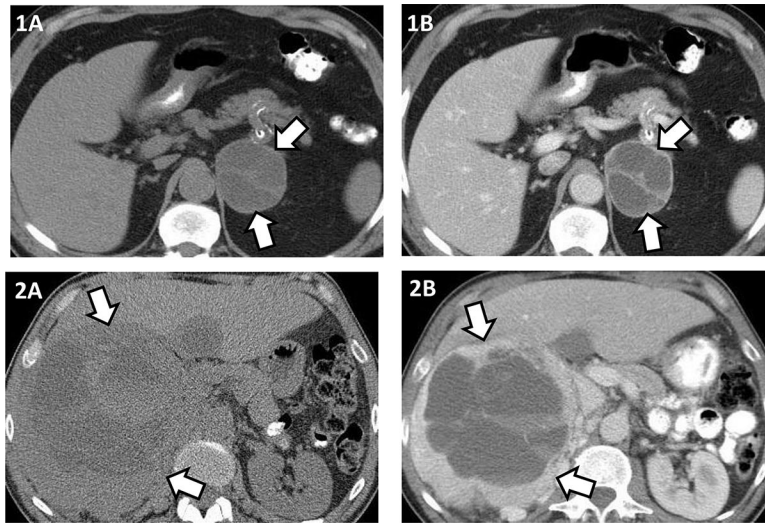
Figure 2: Illustrating cystic pheochromocytoma appearance on unenhanced and contrast enhanced computed tomography (CT).

1A and 1B – Left 6.4 cm pheochromocytoma, cystic component 14 HU, solid component 34 HU on unenhanced CT (**1A**); cystic component 20 HU, solid component 90 HU, rim and septal enhancement on contrast enhanced CT (**1B**).

2A and 2B –Right 18.9 cm pheochromocytoma, cystic component 18 HU, solid component 35 HU on unenhanced CT (**2A**); cystic component 21 HU, solid component 132 HU, rim enhancement on contrast enhanced CT (**2B**).

Table 1.

Presentation and management of patients with cystic pheochromocytoma

	N=21
Clinical presentation	
Age at diagnosis, years, median (IQR)	57 (51–67)
Women, n (%)	12 (57)
Race, n (%)	
White	18 (86)
Native American	1 (5)
Unknown	2 (10)
Mode of discovery, n (%)	
Incidental	13 (57)
Hormone excess symptoms	5 (24)
Mass effect symptoms	2 (10)
Genetic surveillance	1 (5)
Post-adrenalectomy	1 (5)
Symptoms and signs of catecholamine excess, n (%)	13 (62)
Symptoms and signs, n (%)	
Palpitations	8 (62)
Spells	8 (62)
Paroxysmal hypertension	7 (54)
Sustained hypertension	2 (15)
Genetic testing, n (%)	
Not tested	15 (72)
Tested, negative	3 (14)
Tested, positive	3 (14)
Type of pathogenic variant, n (%)	
VHL	1 (33)
NF1	1 (33)
MEN 2A	1 (33)
Extra-adrenal malignancy, n (%)	7 (33)
Imaging phenotype	
Site, n (%)	
Right	15 (71)
Left	6 (29)
Tumor size, cm, median (IQR)	6.4 (5–11.1)

	N=21
Volume, cm³, median (IQR)	
Total	115 (47.4–654.1)
Cystic component	48.7 (15.6–236.3)
Solid component	61.2 (27.3–186.2)
Composition, %, median (IQR)	
Cystic component	40 (24–60)
Solid component	60 (40–76)
Unenhanced CT attenuation, HU, median (IQR), available for n=16	
Cystic component	17.6 (14.6–20)
Solid component	40 (32.1–44.3)
Enhanced CT attenuation[#], HU, median (IQR), available for n=14	
Cystic component	20.4 (14.9–26.8)
Solid component	83 (83.3–121)
Other imaging characteristics	
Round/oval shape, n (%)	19 (90)
Well defined borders, n (%)	21 (100)
Heterogeneous, n (%)	18 (86)
Rim thickness, mm, median (IQR)	14 (8–22)
Calcification, n (%) available for n=20	3 (15)
Biochemical evaluation	
Preoperative evaluation for catecholamine excess, n (%)	20 (95)
Plasma fractionated metanephrines, nmol/L, median (IQR), available for n=18	
Metanephrine (normal <0.5 nmol/L)	2.7 (0.9–8.7)
Normetanephrine (normal <0.9 nmol/L)	13.2 (3.2–23.6)
Urinary fractionated metanephrine, nmol/day, median (IQR), available for n=16	
Metanephrine (normal < 2028 nmol/day)	15828 (5663–33731)
Normetanephrine (normal < 4913 nmol/day)	22957 (9206–84472)
Urinary fractionated catecholamines, nmol/day, median (IQR), available for n=15	
Epinephrine (normal < 115 nmol/day)	470 (104–1715)
Norepinephrine (normal <473 nmol/day)	1093 (609–6461)
Dopamine (normal <2611 nmol/day)	1222 (975–2126)
Tumor type, n (%)	
Adrenergic	16 (80)
Noradrenergic	4 (20)
Perioperative details	
Preoperative medical therapy, n (%)	20 (95)

	N=21
Alpha-adrenergic blockade	
Number of patients treated, n (%)	20 (100)
Duration, days, median (IQR)	15.5 (10.3–20)
Metyrosine	
Number of patients treated, n (%)	4 (20)
Duration, days, median (IQR)	5 (2.8–8)
Beta-adrenergic blockade, n (%)	17 (85)
Adrenalectomy, n (%)	
Laparoscopic	10 (48)
Open	11 (52)
Duration of hospital stay, days, median (IQR)	4 (2–6.5)
Postoperative complications, n (%)	
Hypotension requiring vasopressors	3 (14%)
Pulmonary edema	1 (5%)
Retroperitoneal hemorrhage	1 (5%)
Postoperative ileus	1 (5%)

Abbreviations – CT: Computed Tomography, HU: Hounsfield Unit, IQR: Interquartile range, *MEN 2A*: Multiple endocrine neoplasia type 2A, *NF1*: Neurofibromatosis type 1, *VHL*: Von Hippel Lindau

[#]Measured during portal venous phase

Table 2.

Individual data of patients with cystic pheochromocytoma

Patient indicator	Demographics and presentation			Catecholamine excess	Imaging presentation				
	Age	Sex	Symptoms	Fold increment > upper normal range	Maximum tumor size, cm	Cystic volume, %	Solid volume, %	Unenhanced HU cystic component	Unenhanced HU solid component
A	42	F	Yes	>10	11.2	75	25	30	48
B	50	F	No	>10	9.1	77	23	30	50
C	56	M	Yes	>10	11.7	68	32	14	39
D	59	F	Yes	5–10	4.1	26	74	N/A	N/A
E	55	M	Yes	>10	8.2	50	50	20	46
F	63	M	No	<5	2.9	15	85	19	29
G	66	M	No	5–10	3.8	24	76	13	45
H	57	M	Yes	N/A	18.9	40	60	18	35
I	75	M	No	5–10	6.4	53	47	14	34
J	76	F	Yes	>10	5	49	51	17	42
K	69	F	No	<5	12	64	36	N/A	N/A
L	55	F	Yes	>10	8.2	28	72	17	43
M	86	M	No	<5	5.5	44	56	18	28
N	52	F	Yes	>10	6.5	29	71	N/A	N/A
O	65	F	No	5–10	4.4	24	76	17	32
P	4	M	Yes	>10	5	24	76	27	41
Q	49	M	Yes	>10	13.5	23	77	17	34
R	68	F	Yes	5–10	6.3	25	75	N/A	N/A
S	65	F	No	>10	14.9	22	78	20	44
T	54	F	Yes	<5	5.7	56	44	14	22
U	41	F	Yes	>10	6.3	70	30	N/A	N/A

Abbreviations – F: Female, HU: Hounsfield Unit, M: Male, N/A: Not available

Table 3:

Comparison between cystic and noncystic pheochromocytoma

	Cystic pheochromocytoma	Non-cystic Pheochromocytoma[*]
Median age, years (range)	57 (51–67)	52 (5–84)
Women, (%)	57%	52%
Mode of discovery, %		
Incidental	60%	62%
Abdominal mass effect	25%	-
Symptoms of hormone excess	10%	26%
Genetic surveillance	5%	12%
Symptoms of catecholamine excess regardless of the mode of discovery, %	62%	68%
Type of clinical manifestations, %		
Palpitations	62%	56%
Spells	62%	37%
Paroxysmal hypertension	54%	40%
Sustained hypertension	15%	-
Headaches	-	43%
Tumor laterality, %	Predominantly unilateral	Predominantly unilateral, bilateral in 8%
Median tumor size, cm (range)	6.4 (3–19)	4.0 (8–26)
Median unenhanced CT attenuation, HU (range)	Cystic component: 18 (13–30) Solid component: 40 (22–50)	35 (18–58)
Median contrast enhancement, HU (range)	Cystic component: 20 (15–33) Solid component: 93 (67–132)	83 (22–187)
Biochemical profile, %		
Adrenergic	80%	66%
Noradrenergic	20%	30%
Nonfunctioning	0%	4%
Median total plasma metanephrines, nmol/L (range)	14.3 (3–223)	Median of 2.2–12.4 (0.4–397)[#]
Median total urinary metanephrines, nmol/L	43000 (10030–494681)	Median of 6849–23176 (221–674816)[#]
Adrenalectomy, %		
Laparoscopic	48%	76%
Open	52%	24%
Median hospital-stay following surgery, days (range)	4 (1–17)	3 (1–32)

Abbreviations – CT: Computed Tomography, HU: Hounsfield Unit

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Data from Gruber LM, Hartman RP, Thompson GB, et al. Pheochromocytoma Characteristics and Behavior Differ Depending on Method of Discovery. *J Clin Endocrinol Metab.* 2019;104(5):1386–1393.

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Previously reported stratified based on mode of discovery, lowest in patients discovered based on genetic case detection, and highest in patients presenting with symptoms of catecholamine excess. Presented as range of medians.