Radiology Case Reports 19 (2024) 6152–6156

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Incidental detection of purely cystic pheochromocytoma in a young adult presenting with lower urinary tract infection ☆

Neha Singh, MD[a], *Kishan Kumar Thakur, MD*[a,*], *Shalikh Moidu, MCh*[b], *Nidhi Anand, MD*[c]

[a] *Department of Radiodiagnosis & Imaging, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India*
[b] *Department of Endocrine Surgery, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India*
[c] *Department of Pathology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, India*

ARTICLE INFO

Article history:
Received 23 June 2024
Revised 26 August 2024
Accepted 28 August 2024

Keywords:
Purely cystic pheochromocytoma
Hypertension
Adrenal cyst
Case report

ABSTRACT

Pheochromocytoma is a rare neuroendocrine tumor arising from adrenal medulla. Patients usually show classic triad of headache, palpitations and diaphoresis along with persistent or paroxysmal hypertension. Majority of the tumors are solid or mixed solid and cystic. But purely cystic variant is extremely rare with few cases reports available in the published literature. We report a case of purely cystic pheochromocytoma in a male in 30s who presented to our hospital for unrelated symptom of recurrent burning micturition. He was evaluated for causes of recurrent UTI which revealed incidental right adrenal cyst. The patient's blood pressure was raised on clinical examination and imaging showed simple adrenal cyst without solid component or septations. Suspecting possibility of pheochromocytoma, biochemical analysis was done which revealed elevated 24-hour urinary metanephrine. The diagnosis of cystic pheochromocytoma was made. Adrenalectomy was performed showing cystic lesion in the right adrenal region. Histopathology and immunohistochemistry revealed pheochromocytoma with cystic degeneration. Patient's hypertension resolved during the follow up. In conclusion, purely cystic pheochromocytoma must be considered as differential for adrenal cystic lesions, especially when atypical features are present.

Introduction

Pheochromocytomas are neuroendocrine tumor arising from the adrenal medulla or sympathetic ganglia which cause hypersecretion of catecholamines either paroxysmal or permanent [1]. It can present as hypertension or episodes of palpitations, headache or other symptoms or discovered incidentally on imaging [2]. Its prompt diagnosis is important as its resection leads to dramatic improvement and reversal of symptoms

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: anand.kishan@gmail.com (K.K. Thakur).

https://doi.org/10.1016/j.radcr.2024.08.144

and hypertension while missed or delayed diagnosis causes marked morbidity, even mortality [3]. Diagnosis in done typically on the basis of clinical suspicion, catecholamines hypersecretion detection and imaging studies. The detection of plasma free or urinary fractionated metanephrine are considered the gold standard [4]. Imaging studies are performed to determine the location and morphology in clinically manifested phaeochromocytomas. However, in incidentally discovered adrenal masses on imaging, clinical and biochemical tests are done later [5]. Approximately two thirds are solid and one thirds are complex or cystic [6]. Purely cystic pheochromocytomas are extremely rare with few case reports in literature [7]. In a PubMed search for "cystic pheochromocytoma," 302 results were found. For "pure cystic pheochromocytoma," only 3 results were found. Differential diagnosis includes adrenal cyst and pseudocyst [8,9].

We present a case of purely cystic adrenal lesion who presented with unrelated complaints and imaging evaluation revealed right adrenal cystic lesion without any solid component or septations. Biochemical testing suggested the diagnosis of Pheochromocytoma which was confirmed post operatively.

Case presentation

A male in 30s presented with complaint of recurrent burning micturition for 4 months. On clinical examination patient was found to have raised blood pressure but gave no previous history of hypertension. On detailed history taking, he remembered some episodes of unexplained headache and sweating which relieved on medications. He was kept on blood pressure monitoring which showed readings ranging from 140/90 to 130/85 mmHg. Physical examination revealed no significant abnormality. The primary physician ordered ultrasonography of kidneys and urinary bladder for cause of recurrent UTI which showed incidental cystic lesion in the right adrenal region. Further contrast enhanced CT of whole abdomen (Fig. 1) was performed which showed a thin- walled right adrenal cystic lesion measuring 4.1 × 3.0 × 3.1 cm with internal fluid attenuation of 11-12 Hounsfield units (HU) without enhancing solid component or septations. Considering the hypertensive status of the patient, differential diagnosis of simple adrenal cyst vs purely cystic pheochromocytoma was kept. Biochemical testing revealed raised 24- hour urine metanephrine (160 micrograms/ 24 hours [normal: 24-96 micrograms/ 24h]) with normal levels of urine normetanephrine and serum cortisol which suggested the diagnosis of pheochromocytoma.

Considering the hypertensive status of the patient, the most probable diagnosis of purely cystic pheochromocytoma was made. The differentials were simple adrenal cyst and pseudocyst.

Patient was given option for both open adrenalectomy and laparoscopic adrenalectomy. He chose the open adrenalectomy. For 1 month, the patient underwent preoperative alpha-adrenergic blockade with prazosin with 24-hour BP monitoring. No rise in BP, nasal congestion or any adverse effect was found. Pre operative blood pressure was around 126/84 mm of Hg. Subsequently right adrenalectomy was done under general anesthesia through right subcostal incision. All abdominal muscles with overlying skin and fascia were cut. Triangular ligament was cut and liver was mobilized. Kocherisation of duodenum was done and right adrenal gland was identified. The cystic nature of the tumor was seen intraoperatively, and careful handling of the lesion was done to prevent catecholamine release and complete excision was done. Hemostasis was achieved and drain was put in situ. Wound was closed in layers with vicryl and monocryl. Post operative examination (Fig. 2) revealed a 37 g (4.5 × 5.0 × 2.1 cm) spherical fluctuant cystic mass. Gross histologic examination showed compressed adrenal tumor at the periphery with a large cystic cavity filled with gelatinous material. Microscopy (Fig. 3) showed tumor was composed of moderately pleomorphic polygonal cells with moderate eosinophilic granular cytoplasm and vesicular nuclei and occasional conspicuous nucleoli. Final histopathological diagnosis was pheochromocytoma with cystic degeneration. Immunohistochemistry showed synaptophysin–positive, Chromogranin–Positive and Melan A- Negative which further confirmed the diagnosis. Patient was discharged after 1 week in satisfactory condition.

Postoperatively, immediately 24-hour Urine metanephrine level dropped to 133 micrograms/24 hours. During 1 month follow up the patient's symptoms resolved, blood pressure was normalized and Urine metanephrine came within normal range (80 micrograms/24 hours). Average blood pressure readings were around 124/80 mm of Hg. The patient had no other complaints during the follow-up.

Discussion

Pheochromocytoma originate from chromaffin cells in adrenal medulla or sympathetic ganglia which embryologically arise from the neuroectoderm. Around 80-85% cases arise from the adrenal gland called as adrenal pheochromocytoma and 15%-20% cases arise from sympathetic ganglia called as sympathetic paragangliomas [4]. The estimated prevalence of pheochromocytomas is 1:2500 to 1:1650, with an annual incidence between 1000 and 2000 cases, including 100-200 paediatric patients and 100-200 with metastatic disease [10].

They cause catecholamine hypersecretion leading to classic triad of headache, sweating and palpitations in patients with hypertension. Signs and symptoms can be paroxysmal as there can be episodic catecholamine secretion. The catecholamines are stored within in the cells in storage vesicles, and after release, they act upon adrenoreceptors for their manifestation [11]. However, 20-30% cases are clinically asymptomatic in which detection is incidental on imaging for unrelated symptoms. Biochemical test to measure plasma-free or urinary fractionated metanephrine is considered gold standard for the catecholamine hypersecretion detection [4]. So, measurement of catecholamines including metanephrine and normetanephrine should be included for screening and follow up.

Imaging studies are used for morphological and functional characteristics. Ultrasonography, CT and MRI are generally

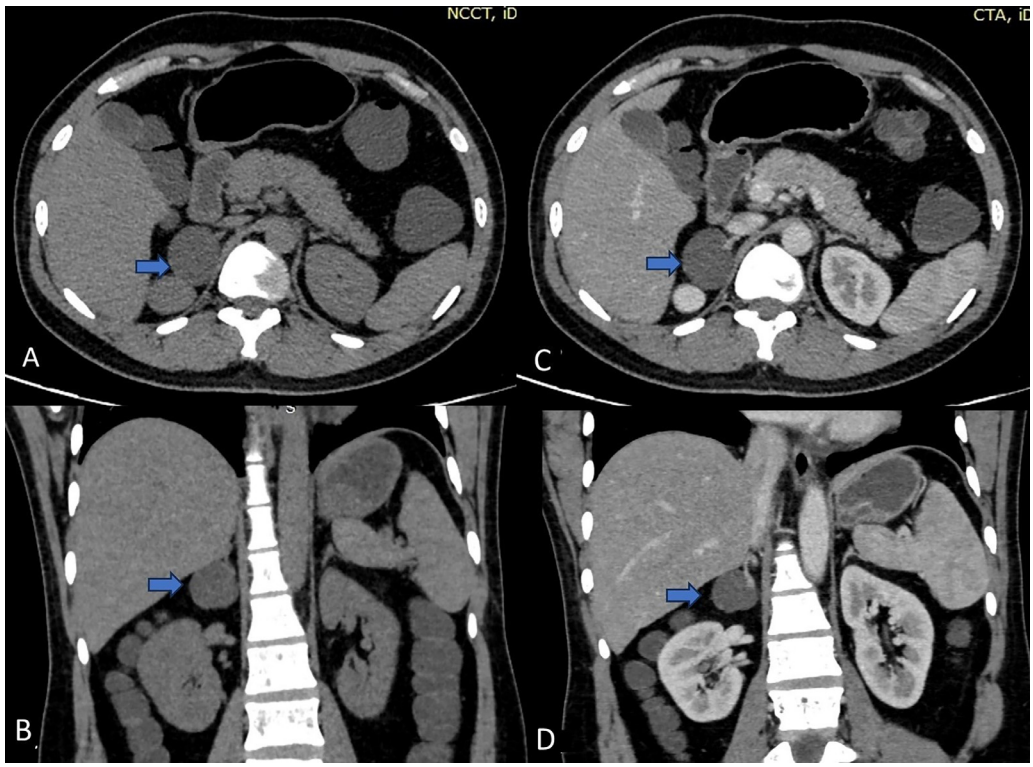

Fig. 1 – Noncontrast (A) axial, (B) coronal and contrast enhanced (C) axial, (D) coronal computed tomography images through the abdomen showing thin-walled cystic lesion in the right adrenal without enhancement, solid component or enhancing septations. (arrows)

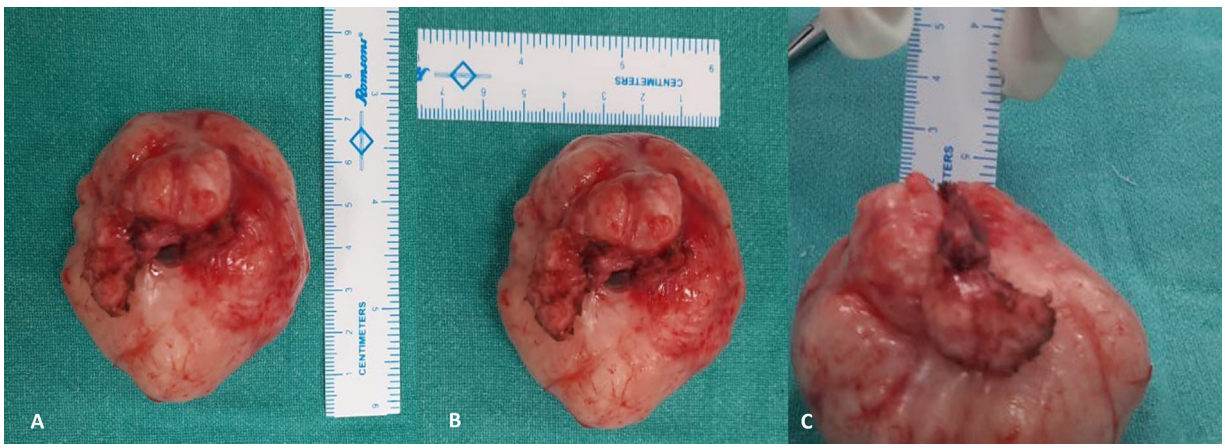

Fig. 2 – Postoperative specimen shows fluctuant cystic mass.

used for anatomic and morphological characteristics. On ultrasound, pheochromocytomas have a variable appearance ranging from solid (75% in 1 case series) to mixed cystic and solid to cystic [12]. The size of the lesion usually varies from 1 to 15 cm [13]. Smaller tumors are generally solid and homogeneous. Larger tumor may show some to marked central necrosis with peripheral rim of tumor tissue. They can mimic other adrenal tumors like adenoma, metastasis or adrenal carcinoma [14]. Pheochromocytomas are usually highly vascular but can develop cystic degeneration, though total cystic degeneration is rare. This process is thought to begin with internal bleeding and necrosis, likely due to the tumor outgrowing its blood supply. The cystic parts of these tumors result from this necrosis and liquefaction, appearing as low attenuation areas on CT scans [15]. Purely cystic pheochromocytomas are a rare subset of a rare tumor, which pose diagnostic and therapeutic challenges. The cystic component can be mistaken for other adrenal lesions, such as cystic adrenal neoplasms or hemorrhage into an adrenal mass and delay the diagnosis. In patients with nonspecific symptoms and incidental adrenal

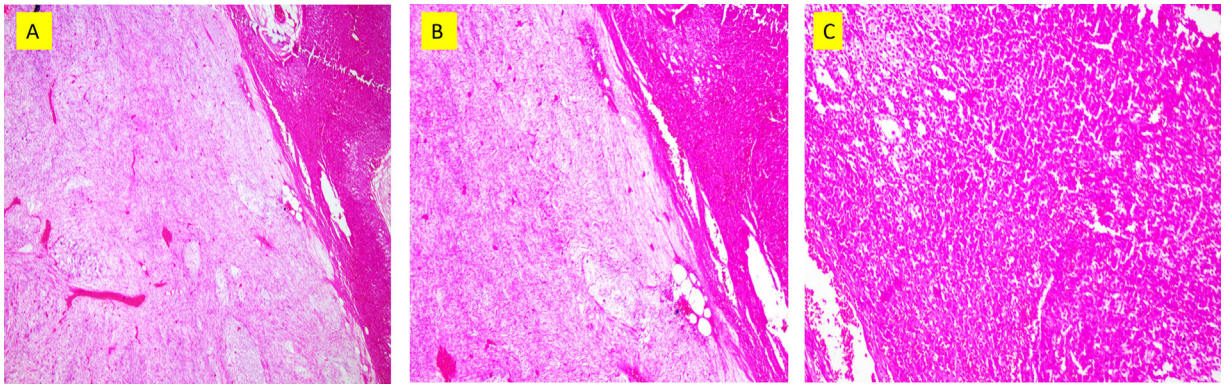

Fig. 3 – Microphotographs (A and B) showing compressed adrenal tumor at the periphery with a large cystic cavity filled with gelatinous material (H&E X20, X40) and (C) showing tumor is composed of moderately pleomorphic polygonal cells with moderate eosinophilic granular cytoplasm (H&E X100).

cystic mass, pheochromocytoma should be considered as differential [16]. However purely cystic pheochromocytoma are difficult to diagnose as they can resemble benign adrenal cysts and do not show typical features of solid pheochromocytoma [4]. In a study conducted by Ito et al. [17], it was found that among 84 patients with Pheochromocytoma (PCC), 44% exhibited partial cystic characteristics, while 10% showed highly cystic features. In another study by Adreoni et al. [18], in comparison to the patients diagnosed with solid tumors, it appears that cystic pheochromocytomas are more prone to being asymptomatic and presenting negative evaluations. In every retroperitoneal cystic lesion, cystic pheochromocytoma must be included in the differential for prompt diagnosis and proper management [19].

Computed Tomography (CT) is the method most commonly used due to its availability, affordability and spatial resolution with the drawback of ionising radiation [1]. Adrenal pheochromocytoma lesions larger than 5-10 mm can be seen on CT with sensitivity of >95% [20]. They can be differentiated from adrenal adenoma readily from adenomas as pheochromocytomas have always higher attenuation >10 HU [21]. This is due to the lack of intracytoplasmic lipids in the pheochromocytoma tumors. Adrenal CT protocols are also used to see late enhancement and washout status. Usually, adrenal adenomas show rapid washout and pheochromocytoma show slower washout [22]. But according to a study, there may be considerable overlap seen as up to 33% of pheochromocytoma showing washout similar to adenoma [23]. Rozenblit et al. categorized cystic adrenal lesions using CT into 3 groups: uncomplicated, complicated, and indeterminate. Uncomplicated lesions are typically smaller than 6 cm, with homogeneous near-water attenuation and thin walls. Indeterminate lesions are larger, with higher attenuation values or thicker walls. Complicated lesions exhibit various characteristics like high attenuation, heterogeneous texture, or calcifications. Surgical intervention is usually needed for complicated and indeterminate lesions, especially to rule out pheochromocytomas and prevent hypertensive crises [24]. MRI is usually not first line investigation, but can be used in pregnant women, children or patients with adverse reaction to iodinated contrast. The signal characteristics of pheochromocytomas on T1 and T2 weighted imaging depends of the lesion morphology whether solid, cystic, necrotic or hemorrhagic.

The molecular imaging methods can be used for functional imaging after obtaining anatomic morphological imaging. Commonly used tests are 123I-MIBG scintigraphy, ^{18}F-FDG or ^{18}F-DOPA PET/CT and somatostatin receptor imaging. The European Association of Nuclear Medicine recommends that the patient's genetic background may be used to select the functional imaging [25].

The definitive treatment for the pheochromocytoma is surgical excision also called as adrenalectomy. Needle biopsy is avoided in suspected pheochromocytoma and surgery is directly done. To reduce the risk of complications during surgery and perioperative mortality, pharmacological management is done preoperatively [26]. Usually, at least 14 days alpha-blocker is required to prevent vasoconstriction. Additionally, beta blocker can be used, but not before, along with alpha-blocker to prevent tachycardia.1 During the surgery, early occlusion of the vein draining the adrenal medulla is performed to prevent the release of catecholamines in the circulation.

After the surgery there should be regular follow up. The long-term prognosis is excellent but hypertension may persist due to residual or metastatic disease [27]. A meta-analysis estimated recurrence rate as low as 3% after mean follow up of 6 years 5 months [28].

In conclusion, multimodal imaging, multidisciplinary approach and biochemical testing are essential for this uncommon purely cystic pheochromocytoma for the prompt diagnosis and appropriate preoperative management to reduce the risk of intraoperative hypertensive crisis.

Conclusion

A comprehensive, multimodal, and multidisciplinary approach is crucial for evaluating adrenal cystic lesions to effectively rule out cystic pheochromocytoma and mitigate the risk of delayed diagnosis and intraoperative hypertensive crises. While classical signs and symptoms may be absent, biochemical markers play a vital role in confirming the diagnosis.

Purely cystic pheochromocytoma, though uncommon, should be considered in the differential diagnosis when imaging reveals a simple adrenal cyst, even if the patient presents with symptoms seemingly unrelated to adrenal function, as illustrated in our case.

Patient consent

Complete written informed consent was obtained from the patient for the publication of this study and accompanying images.

REFERENCES

[1] Čtvrtlík F, Koranda P, Schovánek J, Škarda J, Hartmann I, Tüdös Z. Current diagnostic imaging of pheochromocytomas and implications for therapeutic strategy. Exp Ther Med 2018;15(4):3151–60. doi:10.3892/etm.2018.5871.

[2] Manger WM, Gifford RW Jr. Pheochromocytoma. J Clin Hypertens 2002;4:62–72. doi:10.1111/j.1524-6175.2002.01452.x.

[3] Platts JK, Drew PJ, Harvey JN. Death from phaeochromocytoma: lessons from a post-mortem survey. J R Coll Physicians Lond 1995;29(4):299–306.

[4] Lenders JW, Duh QY, Eisenhofer G, Gimenez-Roqueplo AP, Grebe SK, Murad MH, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2014;99(6):1915–42 Erratum in: J Clin Endocrinol Metab. 2023;108(5):e200. doi:10.1210/jc.2014-1498.

[5] Arnold DT, Reed JB, Burt K. Evaluation and management of the incidental adrenal mass. Proc (Bayl Univ Med Cent) 2003;16(1):7–12. doi:10.1080/08998280.2003.11927882.

[6] Blake MA, Krishnamoorthy SK, Boland GW, Sweeney AT, Pitman MB, Harisinghani M, et al. Low-density pheochromocytoma on CT: a mimicker of adrenal adenoma. AJR Am J Roentgenol 2003;181(6):1663–8. doi:10.2214/ajr.181.6.1811663.

[7] Zhong X, Kokabee M, Sham S, Grasso M, Unger P. Cystic pheochromocytoma: a rare variant of adrenal gland tumor case report. Am J Clin Pathol 2023;160(Supplement_1):S42. doi:10.1093/ajcp/aqad150.094.

[8] Klingler PJ, Fox TP, Menke DM, Knudsen JM, Fulmer JT. Pheochromocytoma in an incidentally discovered asymptomatic cystic adrenal mass. Mayo Clin Proc 2000;75(5):517–20. doi:10.4065/75.5.517.

[9] Rozenblit A, Morehouse HT, Amis ES Jr. Cystic adrenal lesions: CT features. Radiology 1996;201(2):541–8. doi:10.1148/radiology.201.2.8888255.

[10] Crona J, Taïeb D, Pacak K. New perspectives on pheochromocytoma and paraganglioma: toward a molecular classification. Endocr Rev 2017;38(6):489–515. doi:10.1210/er.2017-00062.

[11] Shen Y, Cheng L. Biochemical diagnosis of pheochromocytoma and paraganglioma. Paraganglioma: A Multidisciplinary Approach [Internet]. Mariani-Costantini R, editor editor. Brisbane (AU): Codon Publications; 2019.

[12] Bowerman RA, Silver TM, Jaffe MH, Stuck KJ, Hinerman DL. Sonography of adrenal pheochromocytomas. AJR Am J Roentgenol 1981;137(6):1227–31. doi:10.2214/ajr.137.6.1227.

[13] Jacques AE, Sahdev A, Sandrasagara M, Goldstein R, Berney D, Rockall AG, et al. Adrenal phaeochromocytoma: correlation of MRI appearances with histology and function. Eur Radiol 2008;18(12):2885–92. doi:10.1007/s00330-008-1073-z.

[14] McDermott S, McCarthy CJ, Blake MA. Images of pheochromocytoma in adrenal glands. Gland Surg 2015;4(4):350–8. doi:10.3978/j.issn.2227-684X.2014.11.06.

[15] Munden R, Adams DB, Curry NS. Cystic pheochromocytoma: radiologic diagnosis. South Med J 1993;86(11):1302–5. doi:10.1097/00007611-199311000-00029.

[16] Erem C, Kocak M, Onder Ersoz H, Ersoz S, Yucel Y. Epinephrine-secreting cystic pheochromocytoma presenting with an incidental adrenal mass: a case report and a review of the literature. Endocrine 2005;28(2):225–30. doi:10.1385/endo:28:2:225.

[17] Ito Y, Obara T, Yamashita T, Kanbe M, Iihara M. Pheochromocytomas: tendency to degenerate and cause paroxysmal hypertension. World J Surg 1996;20:923–7. doi:10.1007/s002689900140.

[18] Andreoni C, Krebs RK, Bruna PC, Goldman SM, Kater CE, Alves MT, et al. Cystic phaeochromocytoma is a distinctive subgroup with special clinical, imaging and histological features that might mislead the diagnosis. BJU Int 2008;101(3):345–50. doi:10.1111/j.1464-410X.2007.07370.x.

[19] Zhong X, Kokabee M, Sham S, Grasso M, Unger P. Cystic pheochromocytoma: a rare variant of adrenal gland tumor case report. Am J Clin Pathol 2023;160(Supplement_1):S42. doi:10.1093/ajcp/aqad150.094.

[20] Korobkin M, Giordano TJ, Brodeur FJ, Francis IR, Siegelman ES, Quint LE, et al. Adrenal adenomas: relationship between histologic lipid and CT and MR findings. Radiology 1996;200(3):743–7. doi:10.1148/radiology.200.3.8756925.

[21] Ctvrtlík F, Herman M, Student V, Tichá V, Minarík J. Differential diagnosis of incidentally detected adrenal masses revealed on routine abdominal CT. Eur J Radiol 2009;69(2):243–52. doi:10.1016/j.ejrad.2007.11.041.

[22] Kumagae Y, Fukukura Y, Takumi K, Shindo T, Tateyama A, Kamiyama T, et al. Distinguishing adrenal adenomas from non-adenomas on dynamic enhanced CT: a comparison of 5 and 10 min delays after intravenous contrast medium injection. Clin Radiol 2013;68(7):696–703. doi:10.1016/j.crad.2013.01.016.

[23] Schieda N, Alrashed A, Flood TA, Samji K, Shabana W, McInnes MD. Comparison of quantitative MRI and CT washout analysis for differentiation of adrenal pheochromocytoma from adrenal adenoma. AJR Am J Roentgenol 2016;206(6):1141–8. doi:10.2214/AJR.15.15318.

[24] Rozenblit A, Morehouse HT, Amis ES Jr. Cystic adrenal lesions: CT features. Radiology 1996;201(2):541–8. doi:10.1148/radiology.201.2.8888255.

[25] Taïeb D, Timmers HJ, Hindié E, Guillet BA, Neumann HP, Walz MK, et al. EANM 2012 guidelines for radionuclide imaging of phaeochromocytoma and paraganglioma. Eur J Nucl Med Mol Imaging 2012;39(12):1977–95. doi:10.1007/s00259-012-2215-8.

[26] Brunaud L, Nguyen-Thi PL, Mirallie E, Raffaelli M, Vriens M, Theveniaud PE, et al. Predictive factors for postoperative morbidity after laparoscopic adrenalectomy for pheochromocytoma: a multicenter retrospective analysis in 225 patients. Surg Endosc 2016;30(3):1051–9. doi:10.1007/s00464-015-4294-7.

[27] Mamilla D, Araque KA, Brofferio A, Gonzales MK, Sullivan JN, Nilubol N, et al. Postoperative management in patients with pheochromocytoma and paraganglioma. Cancers (Basel) 2019;11(7):936. doi:10.3390/cancers11070936.

[28] Holscher I, van den Berg TJ, Dreijerink KMA, Engelsman AF, Nieveen van Dijkum EJM. Recurrence rate of sporadic pheochromocytomas after curative adrenalectomy: a systematic review and meta-analysis. J Clin Endocrinol Metab 2021;106(2):588–97. doi:10.1210/clinem/dgaa794.