Case Report

Adrenal Incidentaloma: Challenges in Diagnosing Adrenal Myelolipoma

Sreedhar Adapa, MD1, Srikanth Naramala, MD2, Vijay Gayam, MD3, Frank Gavini, MD2, Hemant Dhingra, MD4, Florette Kimberly Gray Hazard, MD5, Narothama Reddy Aeddula, MD6, and Venu Madhav Konala, MD7

Abstract
Adrenal myelolipomas (AMLs) are rare benign adrenal tumors, containing adipose and hematopoietic tissue, a result of reticuloendothelial cell metaplasia. Incidence on autopsy has been reported from 0.08% to 0.4%. AMLs are generally considered nonsecretory. The functional aspect of adrenal incidentaloma should be evaluated. In this article, we report a case of a 40-year-old male, who presented with uncontrolled hypertension and renal failure, with imaging revealing an adrenal incidentaloma. He was started on dialysis for acute fluid overload, and workup for pheochromocytoma revealed an elevated serum norepinephrine level of 1181 pg/mL. Free metanephrine and normetanephrine levels were low when checked pre- and post-dialysis. Complete resection of the encapsulated right adrenal mass was performed. Pathology of the adrenal tumor demonstrates an 11.5 × 9.5 × 7.5 cm well-circumscribed, partially encapsulated proliferation of mature adipose tissue with admixed hemopoietic elements consistent with myelolipoma weighing 29.3 g. This case highlights the inclusion of a full metabolic workup for all adrenal incidentalomas, including AML.

Keywords
adrenal myelolipomas, adrenal incidentaloma

Introduction
Adrenal myelolipomas (AMLs) are rare benign adrenal tumors, containing adipose and hematopoietic tissue, a result of reticuloendothelial cell metaplasia. It is sporadic with an overall incidence reported 0.08% to 0.4% at autopsy previously, compared with increased incidence of 10% to 15% recently due to the widespread use of imaging. It involves both the genders equally, mostly unilateral, and usually occurs in the fifth and seventh decades of life. Adrenal incidentalomas (AIs) need mandatory metabolic workup as recommended by guidelines of most endocrine societies. The functional aspect of AI should be evaluated.

Case Report
A 40-year-old male was evaluated with the chief complaint of a 1-week history of testicular and bilateral lower extremity swelling. He was found to be in a hypertensive emergency with a blood pressure of 234/119 mm Hg and needed intravenous antihypertensive medications to control the blood pressure. Other vital signs on presentation were a temperature of 98.4°F, pulse rate of 100 beats per minute, and oxygen saturation of 92% on room air. Physical examination was significant for decreased air entry on bilateral lung bases, bilateral lower extremity pitting edema, and scrotal edema. Past medical history was significant for hypertension, morbid obesity, chronic kidney disease stage 4, and right adrenal mass, which was diagnosed 5 years prior to the presentation (interval increase in the growth on serial computed tomography [CT] scans). The patient has been prescribed multiple antihypertensives but was noncompliant.

Laboratory data showed hemoglobin 8.7 mg/dL, blood urea nitrogen 70 mg/dL, and creatinine 8.7 mg/dL, with glomerular filtration rate 7 mL/min. A CT abdomen/pelvis without...
contrast revealed an interval increase in the size of hypo-
tenuating right adrenal mass measuring 9.7 × 7.7 × 6.1 cm
compared with 8.2 × 6.9 × 6.4 cm 6 months prior (Figure 1).
Other investigations showed increased serum norepinephrine
level 1181 pg/mL (80-520 pg/mL), which was 931 pg/mL
6 months prior; also increased serum dopamine level 31 pg/mL
(0-20 pg/mL), which was <20 pg/mL 6 months prior.
Plasma aldosterone renin ratio and serum cortisol levels
were within normal limits (plasma renin activity 0.9 ng/mL/h
[0.2-1.6 ng/mL/h], plasma aldosterone level 11.3 ng/dL
[4-31 ng/dL], and serum cortisol 12.8 µg/dL [6.7-22.6 µg/dL]).
Prior 24 hours urinary metanephrine/normetanephrine levels
as well as catecholamine levels were inconclusive (normeta-
nephrine 828 µg/d [110-1050 µg/d], metanephrine 412 µg/d,
epinephrine level 12 µg/d [1-7 µg/d], dopamine level 77 µg/d
[77-324 µg/d], and norepinephrine 23 µg/d [16-71 µg/d]).
The patient was started on hemodialysis in the setting of pro-
gressively declining renal function and fluid overload state.
Blood pressure was controlled with multiple antihyperten-
sive medications including amlodipine 10 mg daily, hydral-
zine 100 mg 3 times a day, isosorbide mononitrate 30 mg
sustained release daily, minoxidil 5 mg daily, spironolactone
25 mg daily, phenoxybenzamine 10 mg twice a day, and by
volume removal on dialysis.

The patient was transferred to the tertiary care center due
to the unavailability of the endocrine surgeon. At the tertiary
care center, CT of abdomen and pelvis with contrast revealed
heterogeneously enhancing round adrenal lesion on the
right measuring 9.9 × 8.7 cm. Average attenuation is approx-
imately 0 Hounsfield units (HU), and lesion enhances to 16
HU on venous and delayed-phase imaging, which is less
consistent with pheochromocytoma. There was also little
difference in the pre- and post-dialysis levels of metanephrines,
which questioned the diagnosis of pheochromocytoma.
Given the history of progressively growing adrenal mass, the
decision was made to proceed with adrenalectomy. The
patient underwent open right adrenalectomy and tolerated
the procedure well with no intraoperative hemodynamic
instability. A completely encapsulated adrenal tumor was
removed intact. Pathology of the adrenal tumor demonstrated
an 11.5 × 9.5 × 7.5 cm well-circumscribed, partially encap-
sulated proliferation of mature adipose tissue with admixed
hemopoietic elements consistent with myelolipoma weighing
29.3 g (Figure 2). The patient continues to be dialysis
dependent.

Discussion

Adrenal myelolipoma is a benign tumor originating from the
adrenal cortex and is usually nonfunctional. Gierke initially
described myelolipoma in 1905, and Oberling coined the
term “myelolipomatose” in 1929.2 The tumor is composed
of mature adipose tissue admixture with hematopoietic ele-
ments. AML involving extra-adrenal locations like thorax,
liver, spleen, stomach, mesentery, pelvis, and retroperitoneum
have been reported.1 Rarely they can be functional or coexist
with other endocrine disorders like Cushing syndrome, con-
genital adrenal hyperplasia (CAH), primary aldosteronism,
and pheochromocytoma. CAH has been increasingly reported
with AML.4 Chronic ACTH over stimulation of adrenals may
have a role in patients with bilateral AML and also in patients
with untreated CAH with AML.5

The comorbidities like hypertension, obesity, diabetes,
atherosclerosis, and malignancy have been associated with
AML.6 AML has been reported with thalassemia rarely and
tend to be giant and bilateral, due to increased production of
erthropoietin.7

The origin of AML is unclear; few postulated mechanisms
are extramedullary hematopoiesis, hamartosis, embolism of
bone marrow element, metaplasia of reticuloendothelial cells
of blood capillaries (infections, chronic stress, inflammation,
and necrosis) in adrenal glands, and degeneration of adrenal
cortical cells.7,8 AML is a clonal tumor based nonrandom
X-chromosome inactivation identified on recent cytogenetic
studies.7

Adrenal myelolipoma is usually asymptomatic and gen-
erally has a diameter <5 cm, but can vary from <1 cm to
>30 cm. Sometimes the diameter of AML is >10 cm, often
described as giant AML. Akamatsu et al described the largest
AML without the endocrine disorder, measuring 31 ×
24.5 × 11.5 cm and weighing 6000 g.9 Boudreaux et al
described the largest AML in a patient with CAH, size 34 ×
24 × 10.5 cm, weight 5900 g.10

The serum catecholamine levels are not reliable for the
diagnosis of pheochromocytoma.11 The sensitivity and speci-
cicity of plasma catecholamines are very low at 78.6% and
70.7%, respectively.12 The plasma-free metanephrines or ur-
inary fractionated metanephrines are more sensitive and spe-
cific in pheochromocytoma.13 The CT scan also showed low
Hounsfield units, which are less likely, consistent with
pheochromocytoma.14

Recent American Association of Clinical Endocrinologists
(AACE) disease state clinical review suggested that incident-
ally discovered adrenal masses require dynamic and static
hormonal measurements.15 The previous AACE guidelines
published in 2009 did not recommend metabolic workup for
AML.16 Endocrine dysfunction of AML is underappreciated

Figure 1. Computed tomography scan of the abdomen showing
adrenal myelolipoma measuring 8.2 × 6.9 cm.
as the review of the literature reveals that 7% in AML and 11% in AI were functional. AML should not always be excluded from metabolic workup. Endocrine workup is beneficial in AML patient with hypertension, younger patients, diabetes or prediabetes, and those with bilateral AML. Function AML resection resulted in resolution of hypertension and sequelae in several reports, underestimating the incidence of hormonal abnormality.

Adrenal myelolipoma can be diagnosed in 90% of the cases by ultrasonography, CT, and magnetic resonance imaging. CT is more sensitive for detection than other imaging modalities. Ultrasonography appearance can be hyperechoic or hypoechoic depending on the predominance of fat or myeloid cells. Similarly, CT can have a high attenuation with myeloid tissue and low attenuation with a fatty tumor. Magnetic resonance imaging appearance of the tumor demonstrates the high signal intensity and reduced signal intensity depending on the T1-weighted or T2-weighted sequences, respectively. Retroperitoneal fat–containing tumors like teratoma, lipoma, myelolipoma, angiomyolipoma, and liposarcoma may mimic AML radiologically.

Adrenal biopsy should be considered in the following circumstances as per endocrine literature: (1) hormonal inactivity of the adrenal mass, especially ruling out pheochromocytoma; (2) benign characteristics of an adrenal mass not established on imaging; and (3) biopsy results of adrenal mass would alter the management.

Pathological diagnosis of AML requires the presence of hematopoietic elements and mature adipocytes. Management of AML is dependent on the size of the tumor. Tumors <5 cm are generally asymptomatic and can be monitored intermittently with imaging (1-2 years). Surgical removal is indicated if the patient is symptomatic, tumor >5 cm, increased risk of rupture, or if malignancy is suspected. Spontaneous retroperitoneal hemorrhage is a well-recognized complication of AML, which is rare.

**Conclusion**

This case highlights the inclusion of a full metabolic workup for all adrenal incidentalomas, including AML. The serum catecholamine levels are not reliable for diagnosis of pheochromocytoma, but measured plasma metanephrine levels or urinary fractionated metanephrines are more sensitive and specific in pheochromocytoma.

**Authors’ Note**

An abstract of this article was presented as a poster at the National Kidney Foundation Spring Clinical Meeting, Boston, MA, on May 9, 2019, by the same authors under the title “Functioning Adrenal Myelolipoma: Diagnostic Dilemma With Pheochromocytoma.”

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**Ethics Approval**

Our institution does not require ethical approval for reporting individual cases or case series.

**Informed Consent**

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

**ORCID iDs**

Sreedhar Adapa https://orcid.org/0000-0001-5608-5654
Vijay Gayam https://orcid.org/0000-0001-5194-9134
Venu Madhav Konala https://orcid.org/0000-0003-1953-8815
References

1. Olsson CA, Krane RJ, Klugo RC, Selikowitz SM. Adrenal myelolipoma. Surgery. 1973;73:665-670.
2. Wilhelmus JL, Schrod GR, Alberhasky MT, Alcorn MO. Giant adrenal myelolipoma: case report and review of the literature. Arch Pathol Lab Med. 1981;105:532-535.
3. Akhtar F, Ishiaq S, Ali Z, Hassan U. Adrenal myelolipoma. Ann Pak Inst Med Sci. 2009;5:266-268.
4. Nakayama Y, Matayoshi N, Akiyama M, et al. Giant adrenal myelolipoma in a patient without endocrine disorder: a case report and a review of the literature. Case Rep Surg, 2018;2018:4854368.
5. Kale G, Pelley EM, Davis DB. Giant myelolipomas and inadvertent bilateral adrenalectomy in classic congenital adrenal hyperplasia. Endocrinol Diabetes Metab Case Rep. 2015;2015:150079.
6. Saha M, Dasgupta S, Chakrabarti S, Chakraborthy J. Giant myelolipoma of left adrenal gland simulating a retroperitoneal sarcoma. Int J Adv Med Health Res. 2015;2:122-125.
7. Kumar S, Jayant K, Prasad S, et al. Rare adrenal gland emergencies: a case series of giant myelolipoma presenting with massive hemorrhage and abscess. Nephrourol Mon. 2015;7:e22671.
8. Shenoy VG, Thota A, Shankar R, Desai MG. Adrenal myelolipoma: controversies in its management. Indian J Urol. 2015;31:94-101.
9. Akamatsu H, Koseki M, Nakaba H, et al. Giant adrenal myelolipoma: report of a case. Surg Today. 2004;34:283-285.
10. Boudreaux D, Waisman J, Skinner DG, Low R. Giant adrenal myelolipoma and testicular interstitial cell tumor in a man with congenital 21-hydroxylase deficiency. Am J Surg Pathol. 1979;3:109-123.
11. Elias AN, Vaziri ND, Maksy M. Plasma norepinephrine, epinephrine, and dopamine levels in end-stage renal disease: effect of hemodialysis. Arch Intern Med. 1985;145:1013-1015.
12. Hickman PE, Leong M, Chang J, Wilson SR, McWhinney B. Plasma free metanephrines are superior to urine and plasma catecholamines and urine catecholamine metabolites for the investigation of pheochromocytoma. Pathology. 2009;41:173-177.
13. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:1915-1942.
14. Canu L, Van Hemert JAW, Kerstens MN, et al. CT characteristics of pheochromocytoma: relevance for the evaluation of adrenal incidentaloma. J Clin Endocrinol Metab. 2018;104:312-318.
15. Vaidya A, Hamrahian A, Bancos I, Fleseriu M, Ghayee HK. The evaluation of incidentally discovered adrenal masses. Endocr Pract. 2019;25:178-192.
16. Zeiger MA, Thompson GB, Duh QY, et al. American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons medical guidelines for the management of adrenal incidentalomas. Endocr Pract. 2009;15(suppl 1):1-20.
17. Fassnacht M, Arlt W, Bancos I, et al. Management of adrenal incidentalomas: European society of endocrinology clinical practice guideline in collaboration with the European network for the study of adrenal tumors. Eur J Endocrinol. 2016;175:G1-G34.