



CASE REPORT

Urinary Vanillylmandelic Acid Levels in the Workup of Adrenal Incidentaloma

Iass El-Lakkis, M.D.¹, Rami Mortada, M.D.²,
P. Tyson Blatchford, M.D.³, Justin Moore, M.D.¹

¹University of Kansas School of Medicine-
Wichita, Department of Internal Medicine,
Wichita, Kansas

²University of California-Davis, Division of
Endocrinology, Sacramento, California

³South Central Kansas Regional Medical Center,
Department of Surgery, Arkansas City, Kansas

Introduction

Although the majority of patients with pheochromocytoma have hypertension, 5-15% of patients are normotensive and this percentage may be higher in patients with adrenal “incidentalomas”.¹⁻³ The diagnosis of asymptomatic pheochromocytoma is increasing in incidence, most likely due to widespread use of sectional imaging.⁴ The most reliable method for diagnosing pheochromocytoma or paraganglioma is measurement of 24-hour urine catecholamines and metanephrines, with a sensitivity and specificity of roughly 98%.⁵⁻⁷ The urinary vanillylmandelic acid level though may retain some value in the diagnosis of pheochromocytoma, particularly when paired with characteristic findings on imaging.

Case Report

A 68-year-old male underwent computed tomography (CT) of the abdomen as part of a work-up for back pain and an unintentional 20 pound (9 kg) weight loss over the previous six months. The scan revealed a right-sided adrenal mass 1.8 cm in maximum dimension. A follow-up CT scan after six months showed an increase in the size of the mass to 2.2 x 1.8 cm, with a non-contrast attenuation value of 13 Hounsfield units (HU). The mass was noted to have an irregular border. CT scanning of

the chest was performed and demonstrated no evidence of other masses or adenopathy.

The patient denied fevers, flushing, palpitations, abdominal pain, or other constitutional symptoms. He was a previous smoker, with roughly a 30 pack-year history.

Physical examination and vital signs were normal. Laboratory revealed a normal random serum cortisol of 7 mcg/dl. A 24-hour urine collection for catecholamines and metanephrines was within normal limits, with total metanephrines of 772 mcg/24 hours (normal range 224-832 mcg/24 hours) and catecholamines of 55 mcg/24 hours (normal range 26-121 mcg/24 hours). The 24-hour urine vanillylmandelic acid (VMA) was elevated minimally at 9 mg/24 hours (normal range <9 mg/24 hours). Because of the patient’s weight loss and the history of tobacco abuse, he was scheduled for laparoscopic surgical resection of the mass with malignancy high in the differential diagnosis.

Intraoperatively, the patient developed tachycardia of 140 beats per minute and hypertension, with a systolic blood pressure exceeding 260 mm Hg. He was given IV metoprolol and nitroglycerin with good results.

Pathology revealed a 1.5 cm tumor located in the adrenal medulla and compressing the adrenal cortex, consistent

with a pheochromocytoma. Low mitotic activity was noted. Neither tumor necrosis nor invasion into the periadrenal tissue was noted. Subsequent laboratory analysis,

including a calcitonin level, was normal.

The patient recovered without incident and was discharged on no antihypertensives the day following surgery.

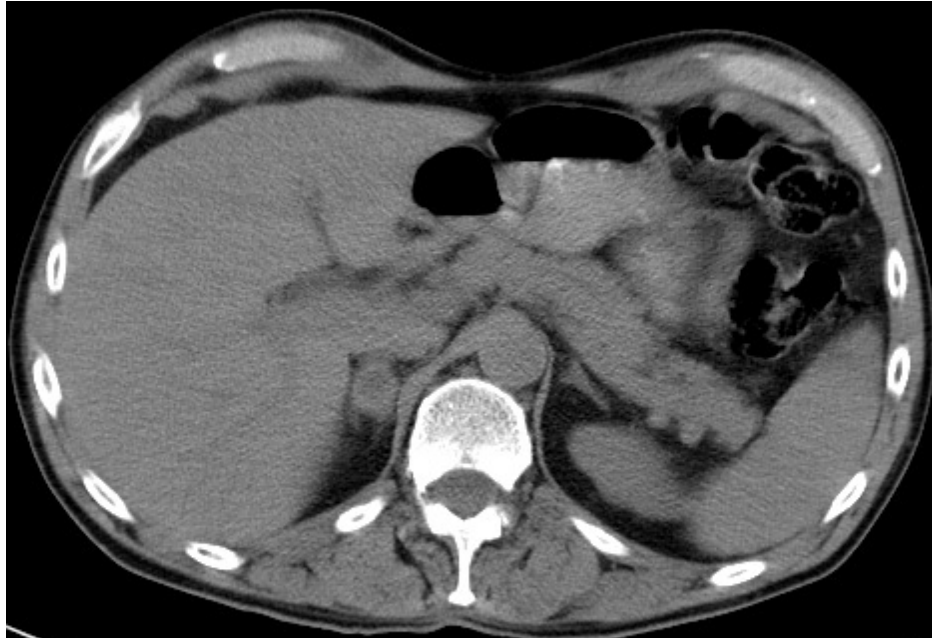


Figure 1. A 1.5 cm tumor located in the adrenal medulla and compressing the adrenal cortex, consistent with a pheochromocytoma

Discussion

Pheochromocytoma may be present in up to five percent of all patients with an adrenal incidentaloma.⁷ Imaging characteristics typically help to differentiate between pheochromocytoma and adrenal adenoma. A Hounsfield attenuation value less than 10 HU on unenhanced CT scanning typically is associated with a benign cortical adenoma. A value of greater than 10 HU is associated with malignancy, pheochromocytoma, and less commonly adenoma (roughly 30 percent of adenomas do not have a large lipid content).⁹

Contrast washout may help differentiate between adenomas and nonadenomas.¹⁰ Typically, adenomas are associated with rapid (> 50 percent at 10 minutes) contrast material washout in contrast-enhanced CT,

whereas carcinomas or pheochromocytomas are associated with delayed (< 50 percent at 10 minutes) contrast material washout.

Beside the patient's slightly elevated urinary VMA and moderately high pre-contrast attenuation, little in our patient suggested the presence of a pheochromocytoma. The indication for surgery was suspicion for malignancy.

The urinary VMA has fallen out of favor as a routine test for pheochromocytoma. The elevated urinary VMA, though, should have changed management of this patient, as it has been shown to have a specificity of 96 percent for the presence of a pheochromocytoma. It is limited by its poor sensitivity of 76 percent.¹¹

Conclusions

We depend on history, physical exam, laboratory, and radiological characteristics to diagnose pheochromocytoma, but sometimes the definitive diagnosis is regrettably established by pathology. The patient's history of weight loss led to the discovery of the neoplasm, but did not prompt the examiners to consider

pheochromocytoma highly on their differential diagnosis. Closer attention to detail in this case, namely, notation of the relatively high attenuation of the lesion in combination with the elevated urinary VMA, may have led to appropriate alpha blockade and thus prevented an intraoperative hypertensive emergency.

References

- ¹ Bravo EL. Pheochromocytoma: New concepts and future trends. *Kidney Int* 1991; 40(3):544-556. PMID: 1787652.
- ² Manger WM, Gifford RW. Pheochromocytoma. *J Clin Hypertens (Greenwich)* 2002; 4(1):62-72. PMID: 1181644.
- ³ Neumann HP, Pawlu C, Peckowska M, et al. Distinct clinical features of paraganglioma syndromes associated with SDHB and SDHD gene mutations. *JAMA* 2004; 292(8):943-951. PMID: 15328326.
- ⁴ Kudva YC, Young WF Jr, Thompson GB, Grant CS, van Heerden JA. Adrenal incidentaloma: An important component of the clinical presentation spectrum of benign sporadic adrenal pheochromocytoma. *Endocrinologist* 1999; 9:77-80.
- ⁵ Kudva YC, Sawka AM, Young WF Jr. Clinical review 164: The laboratory diagnosis of adrenal pheochromocytoma: The Mayo Clinic experience. *J Clin Endocrinol Metab* 2003; 88(10):4533-4539. PMID: 14557417.
- ⁶ Sawka AM, Jaeschke R, Singh RJ, Young WF Jr. A comparison of biochemical tests for pheochromocytoma: Measurement of fractionated plasma metanephrines compared with the combination of 24-hour urinary metanephrines and catecholamines. *J Clin Endocrinol Metab* 2003; 88(2):553-558. PMID: 12574179.
- ⁷ Perry CG, Sawka AM, Singh R, Thabane L, Bajnarek J, Young WF Jr. The diagnostic efficacy of urinary fractionated metanephrines measured by tandem mass spectrometry in detection of pheochromocytoma. *Clin Endocrinol (Oxf)* 2007; 66(5):703-708. PMID: 17388796.
- ⁸ Young WF Jr. Management approaches to adrenal incidentalomas. A view from Rochester, Minnesota. *Endocrinol Metab Clin North Am* 2000; 29(1):159-185, x. PMID: 10732270.
- ⁹ Grumbach MM, Biller BM, Braunstein GD, et al. Management of the clinically inapparent adrenal mass ("incidentaloma"). *Ann Intern Med* 2003; 138(5):424-429. PMID: 12614096.
- ¹⁰ Hamrahian AH, Ioachimescu AG, Remer EM, et al. Clinical utility of noncontrast computed tomography attenuation value (hounsfield units) to differentiate adrenal adenomas/hyperplasias from nonadenomas: Cleveland Clinic experience. *J Clin Endocrinol Metab* 2005; 90(2):871-877. PMID: 15572420.
- ¹¹ Boyle JG, Davidson DF, Perry CG, Connell JM. Comparison of diagnostic accuracy of urinary free metanephrines, vanillyl mandelic acid, and catecholamines and plasma catecholamines for diagnosis of pheochromocytoma. *J Clin Endocrinol Metab* 2007; 92(12):4602-4608. PMID: 17635948.

Keywords: vanillylmandelic acid, adrenal gland neoplasms, pheochromocytoma, case report