Subclinical Pheochromocytoma and Paraganglioma in an Elderly Patient: A Case Report

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Abstract
Pheochromocytomas and paragangliomas are a class of neuroendocrine tumors with a widely variable clinical presentation ranging from paroxysmal episodes of critically elevated blood pressure to no clinical symptoms. Genetic predisposition to pheochromocytomas is well documented. Initial workup entails biochemical evaluation of urine catecholamine metabolites, intravenous contrast enhanced anatomic imaging for adrenal gland evaluation, and functional imaging with methyliodobenzylguanidine (MIBG) whole-body scintigraphy for localization of extra-adrenal disease.

We present an atypical case of concomitant pheochromocytoma and retroperitoneal paraganglioma in an elderly 78-year-old female found to have incidental bilateral adrenal and retroperitoneal masses on abdominal CT since 3 years. Subsequent biochemical workup was consistent with pheochromocytoma. The patient denied any headache, sweating, or palpitations or other suggestive symptoms. She was then lost to follow up for 3 years until she presented to our institution for ischemic leg pain warranting urgent surgical resection of her pheochromocytoma. Following repeat workup and surgical resection, histopathology confirmed right adrenal pheochromocytoma and retroperitoneal paraganglioma. This case is highly atypical of pheochromocytoma given the old age at presentation, subclinical course, and associated paraganglioma, arousing suspicion for familial disease.

ABBREVIATIONS
PHEO: Pheochromocytoma; PARA: Paraganglioma; MIBG: Metyliodobenzylguanidine; CT: Computed Tomography; ACE: Angiotensin-Converting Enzyme; MEN: Multiple Endocrine Neoplasia

CASE PRESENTATION
The patient is a pleasant 78-year-old Caucasian female with a known medical history of hypertension, type 2 diabetes, dyslipidemia, and peripheral vascular disease. She was admitted to our institution for worsening ischemic left foot pain warranting urgent surgical revascularization.

Her peripheral vascular disease goes back to an earlier hospitalization at another institution where she underwent a failed percutaneous intervention. Review of available medical history from that institution also showed she was hospitalized 3 years earlier for acute abdomen on CT found to be due to ileocolic intussusception. The same CT showed incidental bilateral adrenal masses and a retroperitoneal mass. Following surgical treatment of her intussusception, she was referred to endocrinology for evaluation of the adrenal masses. Biochemical workup at the time showed elevated urine metanephrine levels consistent with PHEO. She was then lost to follow-up for the next 3 years but eventually returned to endocrinology for repeat biochemical evaluation, again showing elevated urine catecholamines. Except for left foot pain related to her peripheral vascular disease, she was essentially asymptomatic. She denied ever having episodes of headaches, palpitations, or excessive sweating. She also denied any chest pain, shortness of breath, cough, wheezing, fevers, chills, abdominal pain, nausea, vomiting, or diarrhea. She reported no change in vision or weight, no polyuria, and no polydipsia. Her hypertension was well controlled with a calcium channel blocker and an ACE inhibitor.

Except for an erythematous left lower extremity with absent pulses, the patient’s physical examination, including vital signs, were within normal limits. A detailed review of the clinical laboratory data showed a normal complete blood count and metabolic profile, except for slightly elevated serum blood glucose of 122 mg/dL. The most recent catecholamine levels at the time showed the following parameters to be elevated:

urine norepinephrine 242 mcg/24 hours (normal 15-100 mcg/24 hours), total urine epinephrine and norepinephrine of 255 mcg/24 hours (normal 26-121 mcg/24 hour), urine metanephrine of 1750 mcg/24 hours (normal less than 670 mcg/24 hours), total urine metanephrine and normetanephrine levels 1909 mcg/24 hours (normal less than 832 mcg/24-hour), and serum chromogranin A level of 22 ng/mL (normal 1.9-15 ng/mL).

Urine cortisol levels were within normal limits. Contrast-enhanced CT of the abdomen showed enhancing right adrenal and retroperitoneal masses and a nonenhancing left adrenal gland lesion (Figure 1). MIBG whole-body scan was subsequently performed confirming metabolically active right adrenal PHEO and retroperitoneal PARA (Figure 2). The patient underwent a right adrenalectomy and PARA resection. She tolerated the procedure without incident. Postoperative histopathology confirmed right adrenal PHEO and retroperitoneal PARA with an adjacent benign neuroma (Figure 3).

**DISCUSSION**

PHEOs are a class of sympathetic catecholamine secreting neuroendocrine tumors of neural crest cell origin arising from the adrenal medulla [1]. PARAs are predominantly parasympathetic and nonsecretory, except when they originate from the extra adrenal sympathetic chain ganglia or organ of Zuckerkandl in the abdomen [2].

Most cases of PHEO are sporadic although up to 24% of these cases demonstrated evidence of germline mutations in PHEO susceptibility genes, such as RET, VHL, and NF1 genes [3].

Patients with known MEN II, Von Hippel-Lindau disease, and neurofibromatosis type I have a greater prevalence of PHEO and PARA [4]. Extraadrenal disease was found to be a striking

**Figure 1** Contrast enhanced abdominal CT in axial, coronal, and sagittal projections of the 78 year old female patient demonstrating rim and heterogeneous enhancement of right adrenal pheochromocytoma and retroperitoneal paraganglioma, respectively. Note the lack of contrast enhancement within left adrenal lesion, a pattern most consistent with benign adenoma.

**Figure 2** Planar whole-body MIBG scintiscan revealing intense MIBG accumulation within right adrenal pheochromocytoma and retroperitoneal paraganglioma.

**Figure 3** (A) Hematoxylin and Eosin (H&E) stain of resected right adrenal gland clearly defining thin adrenal cortex and extensive medullary proliferation of cells consistent with phaeochromocytoma. (B and C) H&E and chromogranin stains revealing proliferation and nesting of enterochromaffin cells within resected paraganglioma specimen.
component of hereditary PHEO and PARA [5]. The concomitant presence of neumrma or ganglioneuromia is known to be associated with MEN IIB and von Recklinhausen's disease [6,7].

The clinical presentation for PHEO is highly variable, ranging from paroxysmal episodes of critically elevated blood pressure to no clinical symptoms. Hypertension may be paroxysmal or continuous. Headaches, palpitations, and diaphoresis are the most common presenting symptoms. As with our patient, adrenal incidentalomas could be the presenting finding. Sporadic cases more frequently present with clinical symptoms and develop larger adrenal masses compared with familial forms [8]. A larger adrenal mass would explain the greater sensitivity of CT for sporadic PHEO compared the familial form, even though there is no significant difference in findings between the two groups in terms of elevated catecholamine levels (epinephrine, norepinephrine, dopamine, epinephrine + norepinephrine, metanephrine, and vanillylmandelic acid) or abnormal MIBG scintigraphy [8]. Overall, the mean age at presentation is greater in patients with sporadic PHEO.

Initial treatment is with alpha adrenergic blockers such as phenoxybenzamine for control of hypertension. However, surgical resection remains the definitive treatment. Alpha-adrenergic blockade is continued until the day of surgery for prevention of intraoperative hypertensive crisis.

Our patient had a rather atypical presentation of PHEO in that she was an elderly patient with a subclinical presentation and extraadrenal disease. There was one study that reported pheochromocytoma in a 75 year old patient [9]. Another case report was made of a 71-year old female presenting similarly to our patient [10]. Our patient was 78 years old at the time of diagnosis, and to the best of our knowledge, she may be the oldest reported patient with concomitant PHEO and PARA. Even though no genetic testing has been performed on our patient as of this writing, we highly suspect a familial variant of PHEO in light of the chronic indolent subclinical course and the presence of an associated PARA with a benign neuroma found on resected specimen evaluation. If confirmed to have a familial PHEO, she may well be the oldest patient with such a case.

CONCLUSION

We have uncovered a highly atypical case of a 78 year old patient with subclinical concomitant PHEO and PARA with a high suspicion for familial disease.

ACKNOWLEDGEMENTS

I would like to thank Drs. Sartaj Sandu, MD and Antoine Makdissi, MD from the Department of Endocrinology at University at Buffalo for allowing me to participate in the care of this patient as well as Drs. Tamera Pazos, MD and Hassan Nakhla, MD from the Department of Pathology at University at Buffalo for their clarification of the histopathological findings.

REFERENCES