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Case Report

Unexplained Cachexia as a Presenting Symptom of Pheochromocytoma in a Geriatric Patient

Amélie Nkodo,[1,*] Iris Wu,[1,*] Sarah Hobgood,[2] and Francesco S. Celi[3]

[1]Virginia Commonwealth University School of Medicine, Richmond, VA 23298, USA
[2]Department of Internal Medicine, Division of Geriatrics, Virginia Commonwealth University School of Medicine, Richmond, VA 23298, USA
[3]Department of Medicine, Division of Endocrinology and Metabolism, UConn Health, Farmington, CT 06030, USA

Correspondence: Francesco S. Celi, MD, MHSc, Department of Medicine, Division of Endocrinology and Metabolism, UConn Health, 263 Farmington Ave, Farmington, CT 06030, USA . Email: celi@uchc.edu.
*These authors share co-first authorship of this work.

Abstract

Pheochromocytomas are rare neuroendocrine tumors that may secrete catecholamines, resulting in a wide array of clinical symptoms. While patients classically present with hypertension, headache, diaphoresis, and flushing, these symptoms are present in only 40% of cases. Here, we describe a 70-year-old woman whose predominant symptom was unexplained severe weight loss over a 12-month period associated with fatigue, anxiety, and palpitations at her endocrinologist and geriatrician visits.

Diagnostic imaging was performed to assess for malignancy and demonstrated a 2.0 cm × 2.0 cm left adrenal mass. The diagnosis of pheochromocytoma was confirmed by elevated plasma normetanephrine levels. After a 2-week alpha blockade with doxazosin, the patient underwent robotic left adrenalectomy.

Following surgery, the patient regained weight, and her hypertension also improved significantly. We hope this uncommon clinical presentation in an older adult characterized by weight loss and frailty will increase the awareness of atypical pheochromocytoma symptomatology, particularly in older individuals.

Key Words: pheochromocytoma, geriatrics, cachexia, weight loss, frailty

Abbreviation: CT, computed tomography.

Introduction

Pheochromocytomas and paraganglioma are rare neuroendocrine tumors in the adrenal medulla and chromaffin tissue. Dubbed "the great masquerader," these tumors can secrete catecholamines causing a wide array of symptoms. Most cases occur in the fourth and fifth decades of life, with an estimated incidence of 0.58 cases/100 000 per year worldwide [1].

Pheochromocytomas classically present as a constellation of hypertension, headache, diaphoresis, and flushing. However, these features are present in only about 40% of cases [2]. Hypertension is the most common presenting symptom, with some studies reporting more than 90% of patients had hypertension that was either sustained or paroxysmal [3]. Other nonspecific symptoms can include anxiety, tremulousness, fatigue, and weight loss despite normal appetite [4]. Widely variable clinical presentations can hinder the timely diagnosis of this potentially fatal condition.

This case report documents an atypical clinical presentation of pheochromocytoma in an older adult, whose main symptoms were unexplained weight loss and increased frailty. We hope that the description of this case will increase the awareness of atypical pheochromocytoma presentation, particularly in older individuals.

Case Presentation

A 70-year-old woman was noted during her endocrinology follow-up visit to have unintentional weight loss of 15.7 kg over a 12-month period. Her comorbidities included hypothyroidism, multinodular goiter, type 2 diabetes on target (glycated hemoglobin A_{1c} 6.3%), dyslipidemia, and well-controlled hypertension (96/55 mm Hg). She also established care with a geriatrician at this time, reporting associated symptoms of fatigue, infrequent night sweats, and increased anxiety that she related to severe ongoing life stressors. The patient met several phenotypic criteria for increased frailty, including weight loss of greater than 5% within a year, fatigue, decreased activity tolerance, and slowing gait speed. Her multidisciplinary care team consisting of endocrinology and geriatrics initiated evaluation for frailty and cachexia with the clinical suspicion of occult malignancy.

At the time of initial presentation, her hypertension regimen consisted of amlodipine 5 mg twice daily, losartan-hydrochlorothiazide 100 to 12.5 mg daily, and carvedilol 6.25 mg daily. She had also received age-appropriate health maintenance screenings for colon cancer, breast cancer, and osteoporosis within the past year that were all negative.

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Diagnostic Assessment

The patient was well-appearing and in no acute distress at all visits. No significant findings were noted on the physical exam throughout her workup. Her other vital signs were within normal limits at the initial presentation and during subsequent follow-up appointments.

At the initial assessment, a broad approach was undertaken to work up possible metabolic, rheumatologic, and malignant causes. The comprehensive metabolic panel, complete blood count, antinuclear antibody, erythrocyte sedimentation rate, glycated hemoglobin A_{1c}, aspartate transaminase, alanine transaminase, alkaline phosphatase, total bilirubin, total protein, albumin, calcium, iron panel, and thyroid function panel were not significantly abnormal at a previous visit with the referring endocrinologist. C-reactive protein, rheumatoid factor, complete blood count, comprehensive metabolic panel, antinuclear antibody, cyclic citrullinated peptide antibodies, and thyrotropin were not significantly elevated. A chest x-ray showed increased opacity in the right middle lobe suggestive of pneumonia or atelectasis. A follow-up computed tomography (CT) scan of the chest showed no evidence of consolidation. A CT of the abdomen and pelvis with and without intravenous contrast identified a left adrenal mass measuring 2.0 × 2.0 cm in size and 136 HU (Fig. 1). No other lesions were noted on imaging, making this adrenal mass likely a primary process rather than a malignant metastasis.

Owing to complaints of heart palpitations, the patient was placed on a cardiac event monitor for 2 and a half weeks. The monitor showed occasional junctional escape beats but no other abnormalities. Further laboratory tests were investigated to work up the identified left adrenal mass. The plasma renin activity and upright aldosterone were 4.572 ng/mL/h (108.36 pmol/L/h), reference range 0.17 to 5.38 ng/mL/h, and 19.0 ng/dL (527.06 pmol/L), reference range 0.0 to 30.0 ng/dL, respectively. The plasma normetanephrines 813.2 pg/mL (4.272.7 pmol/L), reference range less than 145 pg/mL, were more than 2.5 times the upper limit of normal, consistent with pheochromocytoma. The low-dose β blocker was not considered sufficient to cause a significant secondary elevation in metanephrine. Magnetic resonance imaging of the abdomen with and without contrast confirmed the presence of a 1.9 cm × 1.5 cm homogeneously enhancing left adrenal lesion (Fig. 2). Biopsy was deemed unnecessary, and indeed contraindicated in this patient with laboratory evidence sufficient to confirm a diagnosis of pheochromocytoma.

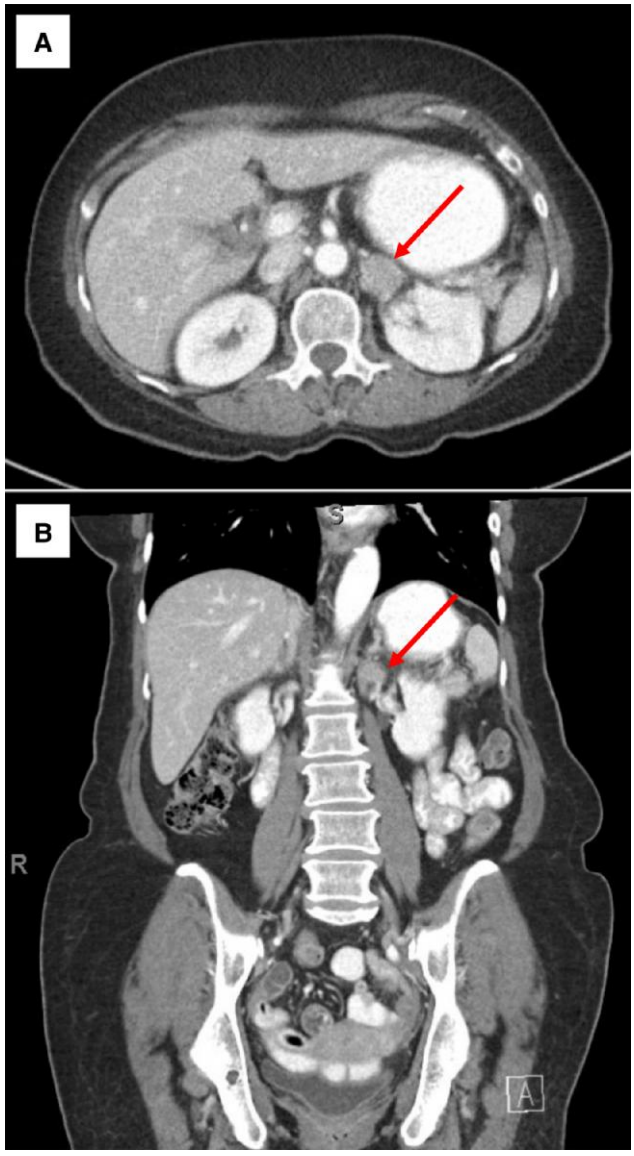

Figure 1. Computed tomography of the abdomen and pelvis with intravenous contrast showing a 2.0 cm × 2.0 cm left adrenal mass. A, Transverse view. B, Coronal view.

Treatment

The diagnostic evaluation spanned 6 months, during which the patient's blood pressure exhibited considerable lability, fluctuating from 104/63 to 163/105 mm Hg. Her amlodipine dosing was adjusted several times, first decreasing from 10 mg daily to 5 mg daily, and finally increasing back to 5 mg in the morning and 2.5 mg in the evening. Once the diagnosis of pheochromocytoma was confirmed, the patient was referred to a surgical oncologist and a left adrenalectomy was scheduled. Doxazosin alpha blockade was initiated 2 weeks before her operation, starting with 2 mg nightly for 1 week, then transitioning to 2 mg twice daily for the second week. She was also instructed to increase her salt intake to assist with volume expansion before surgery. Of her home medications, only losartan-hydrochlorothiazide was held preoperatively. A robotic-assisted left adrenalectomy was performed without any intraoperative complications.

Outcome and Follow-up

While recovering in the postanesthesia care unit, the patient developed transient hypotension and was briefly transferred to the surgical intensive care unit for hemodynamic monitoring. Her remaining antihypertensive agents, amlodipine and carvedilol, were held at this time. On postoperative day 2, she was deemed stable for discharge home. Her hypothyroidism, diabetes, and hyperlipidemia regimens were resumed without change. Of her prior antihypertensive agents, only carvedilol 6.25 mg daily was resumed on discharge.

Subsequent follow-up appointments with her surgeon, endocrinologist, and primary care physician documented that the patient was recovering remarkably well. Her hypertension had improved significantly after the operation,

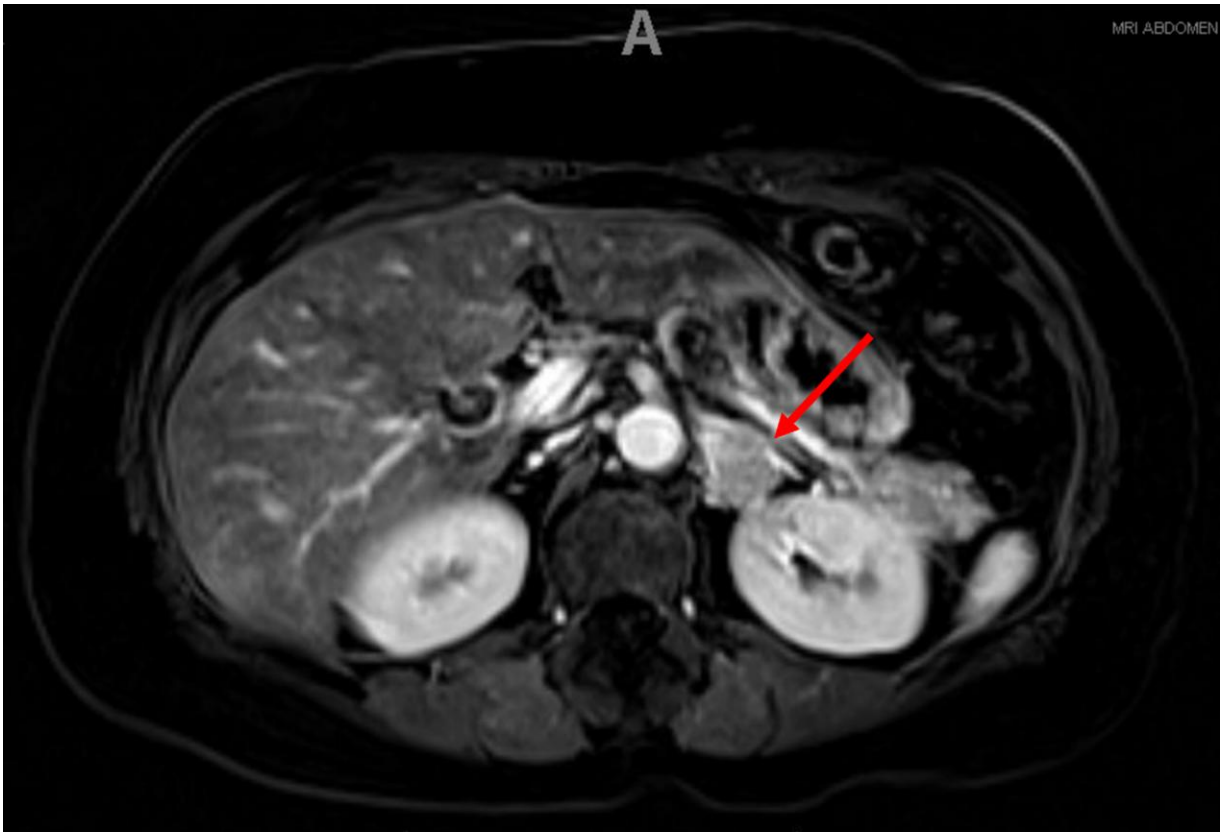

Figure 2. Magnetic resonance imaging of the abdomen showing a 1.9 cm × 1.5 cm homogenously enhancing left adrenal lesion.

remaining well controlled with carvedilol monotherapy. Palpitations had also resolved. Overall, she tolerated the left adrenalectomy well and showed substantial symptomatic improvement afterward. At the last follow-up 2.5 months postoperatively, her weight was 58.4 kg from a nadir of 51.7 kg.

Discussion

This clinical case describes a 70-year-old woman with pheochromocytoma presenting as unexpected weight loss and increased frailty. Here, we have defined frailty as an increased vulnerability to adverse outcomes after exposure to a stressful event. Our patient reported severe life stressors at the time of presentation and exhibited many phenotypic features of frailty such as weight loss, fatigue, decreased activity levels, and slowed gait speed. We did not measure grip strength as an indicator of weakness, which is another aspect of frailty. Several different disease processes can present with increased frailty in an older adult. A thorough workup was undertaken to elucidate the etiology of unexplained weight loss and frailty in this geriatric patient.

Because of the lack of classical signs and symptoms such as refractory hypertension, and because of the age of the patient, a pheochromocytoma was initially low on the differential. The patient's chronic disease status and medication list were meticulously reviewed. Other causes such as depression, dementia, and malignancy were also thoroughly investigated. Ultimately, increased plasma normetanephrine paired with abdominal CT and magnetic resonance imaging evidence of a left adrenal mass confirmed the diagnosis of pheochromocytoma. Not unlike apathetic hyperthyroidism in the geriatric population, this case may be described as an "apathetic pheochromocytoma," where an atypical presentation, such as increased frailty, may make diagnosis more challenging in older adults. In these patients, the diagnostic assessment must rule out a primary adrenal malignancy and secondary adrenal metastases. Important sites to look for primary lesions include the kidney, lung, melanoma and colon, which exhibit frequent metastatic tropism for the adrenal glands. Biopsy of an adrenal mass is rarely needed and should be undertaken with extreme caution. In our patient with clear catecholamine elevation, a biopsy was unnecessary to establish a diagnosis, and indeed contraindicated because of the risk of triggering a catecholamine storm. Similarly, if a primary adrenocortical carcinoma is suspected, great care should be taken since biopsy of the mass can result in seeding of the abdomen with malignant cells.

Several studies have detailed the effect of catecholamines on energy metabolism. For instance, the resting energy expenditure in patients with a pheochromocytoma was higher than predicted values indicating a hypermetabolic state, which normalized following the resection of the neuroendocrine mass [5]. Several studies have shown brown adipose tissue activation, an important regulator of energy metabolism, by tumor-secreted catecholamines, and there is evidence that increased brown fat activation is associated with decreased survival [6]. Therefore, the monitoring of weight changes is important both for the diagnosis and management of pheochromocytomas.

Our patient's laboratory data showed elevated plasma normetanephrines with normal levels of metanephrine, consistent with selective norepinephrine secretion. Her primary complaint of weight loss with these clinical data are consistent

with prior studies indicating that elevated normetanephrines are more strongly associated with weight loss than other catecholamines [7]. Clinically, small studies have shown that normalization of normetanephrines can be used as a predictor of weight gain following surgery [8]. We did not perform a formal evaluation of sarcopenia by dual-energy x-ray absorptiometry because of the lack of body composition software packaging in our clinical setting.

The Endocrine Society recommends genetic testing of patients with pheochromocytoma, as more than one-third of all patients with pheochromocytoma or paraganglioma can have disease-causing germ-line mutations, which can be familial [9]. This option was offered to our patient, who declined as she had no family history of this condition and was not in reproductive age.

Our patient was treated with surgical resection of the left adrenal mass. Following surgery, the patient's blood pressure control was maintained on monotherapy treatment with low-dose carvedilol. Additionally, consistent with the literature on weight loss in the setting of pheochromocytomas, the patient's weight has since stabilized [10]. Overall, this patient's case has an excellent prognosis.

Learning Points

- Excess of catecholamines from pheochromocytomas/paraganglioma induces a hypermetabolic state characterized by weight loss.
- Normetanephrines are most strongly associated with weight loss compared to other catecholamines. Normalization of levels following treatment is associated with weight gain.
- Geriatric patients with unexplained weight loss leading to cachexia should be evaluated for possible neuroendocrine etiologies that may mimic the symptoms of malignancies.

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Contributors

All authors made individual contributions to authorship. S.H. and F.S.C. were involved in the diagnosis and management of this patient and manuscript submission. I.W. and A.N. were responsible for case report writing and literature review. All authors reviewed and approved the final draft.

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Disclosures

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Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

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