CASE REPORT

Lateralizing Sensorimotor Deficits in a Case of Pseudopheochromocytoma

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Pseudopheochromocytoma is a poorly understood, rare cause of severe paroxysmal hypertension that mimics the symptomatology of pheochromocytoma in the absence of biochemical evidence of this tumor. Symptoms such as headache, nausea, sweating, and palpitations during hypertensive episodes have been described. In this paper, we describe previously unreported findings of lateralizing sensorimotor deficits in a patient with pseudopheochromocytoma. These changes presented during a hypertensive episode and were concerning for stroke but were not accompanied by acute radiologic abnormalities. The deficits improved over 1.5 weeks as blood pressure stabilized with beta-blockade. We also review relevant literature on the clinical features, pathophysiology, and management of pseudopheochromocytoma.

INTRODUCTION

Pseudopheochromocytoma is a condition characterized by episodes of paroxysmal hypertension that occur in the absence of biochemical evidence of pheochromocytoma. These paroxysms are accompanied by symptoms of catecholamine excess such as sweating, nausea, headache, dizziness, and palpitations despite normal catecholamine levels in most cases. Although generalized weakness has previously been reported as a symptom in the literature, to our knowledge, lateralizing motor or sensory deficits have not yet been described. Here, we report a case of pseudopheochromocytoma in which sensorimotor changes suggestive of stroke presented during an episode of severe paroxysmal hypertension.

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†Abbreviations: ADHD, attention deficit hyperactive disorder; BMI, body mass index; CK-MB, creatine kinase-MB; CT, computed tomography; EKG, electrocardiogram; GERD, gastroesophageal reflux disease; MRI, magnetic resonance imaging; PTH, parathyroid hormone; PTSD, post-traumatic stress disorder; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TSH, thyroid stimulating hormone.

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CASE PRESENTATION

A 54-year-old Caucasian woman presented to the emergency department after being found to have a systolic blood pressure over 190mm Hg accompanied by nausea at her primary care physician’s office. She reported that during the previous week she had been experiencing sudden, unprovoked episodes of dull chest pain radiating to the back accompanied by dizziness, a throbbing headache, tremulousness, and profuse sweating. She denied diarrhea. Self-measured systolic blood pressures during these episodes were around 180mm Hg.

Her past medical history was significant for gastroparesis, gastroesophageal reflux disease (GERD†), asthma, arthritis, and chronic ankle pain. She noted that she had hypertension prior to significant weight loss in 2012, but since then had not had hypertension and was off all antihypertensive medications. Her past surgical history was notable for orthopedic surgery with hardware placement in her left ankle and both shoulders, as well as what she referred to as an “all in one” surgery in 2012 that included a cholecystectomy, Heller myotomy, and fundoplication. According to the patient, this surgery was complicated by a vagal nerve injury that resulted in gastroparesis and required jejunostomy tube feeding for 13 months, with a weight loss of more than 50 pounds. Prior to admission, she was taking pantoprazole for GERD, hydromorphine for chronic ankle pain, and lorazepam for anxiety on an as-needed basis. Her social history was notable for significant physical and verbal abuse as a child and adult, but she denied alcohol, tobacco, and illicit drug use.

On admission, she appeared thin (BMI=18.3), mildly distressed, and anxious. Her blood pressure was 170/108, and she complained of a headache. No abnormalities were detected on the initial physical exam (including an eye exam) or biochemical tests, and a myocardial infarction was ruled out by negative troponin, creatine kinase-MB (CK-MB), and electrocardiogram (EKG). Over the next few days, she had labile blood pressures while awake and asleep, with systolic blood pressure ranging from 100 to 200mm Hg. During hypertensive episodes, her heart rate increased to above 130 beats per minute, and she complained of nausea, dizziness, and headache. Flushing was not observed.

For management, intravenous labetalol was given during acute episodes. Additionally, phenoxybenzamine and metoprolol were administered out of concern for pheochromocytoma. After pheochromocytoma was ruled out, phenoxybenzamine was discontinued.

Over the course of the hospitalization, the patient was evaluated for secondary causes of hypertension, such as hormone-secreting tumors, by checking the renin-to-aldosterone ratio, 24-hour urine metanephrines, and serum metanephrines, which were all within the normal range. Additionally, urinalysis, thyroid stimulating hormone (TSH), and parathyroid hormone (PTH) were normal. A normal head computed tomography (CT) and carotid Doppler lowered the likelihood of a neurologic etiology. A renal Doppler was negative for renal artery abnormalities. Urine toxicology screen was positive for opiates and benzodiazepines only, as expected from home medications.

On day 6 of admission, the patient was noted to be hypertensive with a blood pressure of 210/120, and a neurological exam revealed new left-sided 4+/5 weakness of proximal and distal muscles, drift of the left upper and lower limbs, abnormal heel-to-shin and questionable facial asymmetry, which had not been noted on prior exams during the hospitalization. Reflexes were 2+ and symmetric throughout. Sensory defects to light touch were present on the left side. Although she appeared drowsy, she was oriented and not confused. No new inpatient medications (metoprolol, phenoxybenzamine) could explain the deficits. A stat head CT followed by a magnetic resonance imaging (MRI) 3 days later (after verifying MRI-compatibility of orthopedic hardware) showed no acute abnormalities such as stroke or hypertensive encephalopathy, despite persistence of sensorimotor abnormalities.
Considering her social history of abuse, a psychiatry consult was called for the possibility of a somatoform disorder. The patient was noted to have an “even-keeled” personality and to display inappropriate affect at times, showing a half-smile regardless of the gravity of the discussion. Regarding her developmental history, she experienced physical and verbal abuse by her stepmother as a child but denied ever having symptoms of post-traumatic stress disorder (PTSD). As an adult, she had two previous divorces to physically and verbally abusive men and was currently in her third marriage without problems. She shared that her son had autism, attention deficit hyperactive disorder (ADHD), and bipolar disease and had recently been incarcerated for breaking into buildings to fund his drug habit. The patient commented that she felt relieved her son was in a safer place. While psychotropic medications and psychotherapy were discussed as treatment options for pseudopheochromocytoma, she was unwilling to pursue them.

Over 1.5 weeks, a stable blood pressure (ranging 112-130/70-80 mm Hg) was eventually achieved on metoprolol, resulting in a cessation of episodes during the hospitalization. Her symptomology improved, and she was discharged.

**DISCUSSION**

We have presented a case of a patient who experienced severe paroxysmal hypertensive episodes associated with various symptoms and lateralizing sensorimotor changes suggestive of a stroke. Before arriving at a presumed diagnosis of pseudopheochromocytoma for this patient, a wide differential was considered, the most concerning of which was pheochromocytoma. However, the finding of normal levels of plasma-free metanephrines (even from a sample collected during an episode) and 24-hour urine metanephrines made the diagnosis unlikely, as the sensitivity of plasma-free metanephrines has been reported to be 99 percent and the specificity of urine total metanephrines to be 93 percent [1].

Since the patient reported having headaches during these episodes at home, we questioned whether headaches were causing the hypertensive paroxysms. However, during her hospitalization, she sometimes had episodes without a headache, but never a headache without an episode, suggesting that the headaches were a symptom and not the cause.

Negative findings on carotid Doppler and brain imaging ruled out brain etiologies, and normal renal Doppler findings, creatinine levels, and renin-to-aldosterone ratio made renal disease less likely. Normal levels of TSH and PTH ruled out thyroid and parathyroid disease, respectively. Although stimulants and drug withdrawal can cause similar symptoms [2], she denied taking illicit drugs or sympathomimetics. Furthermore, the continuation of hypertensive episodes even under close observation in an ICU setting reduced the likelihood of surreptitious use of substances that can affect blood pressure.

Carcinoid syndrome was considered; however, in the absence of diarrhea and flushing, which are present in 70 percent and 75 percent of carcinoid cases [3], its likelihood was lower. Additionally, carcinoid syndrome usually causes hypotension rather than hypertension [4], thus further biochemical testing was not performed. Obstructive sleep apnea has also been shown in case reports to be associated with symptoms suggestive of pheochromocytoma, but patients in these reports had elevated 24-hour urine catecholamines or metanephrines and were obese, unlike our patient [5-7]. Moreover, while baroreflex failure due to possible vagal nerve injury from previous surgery was considered as a cause of labile blood pressure in our patient, it was thought to be unlikely, especially if the injury was unilateral and subdiaphragmatic.

In panic disorder, similar symptoms including headache, weakness, sweating, and palpitations can be observed with blood pressure elevation. However, panic attacks differ in that blood pressure rises only by approximately 20mm Hg on average [8], whereas 40 to 100mm Hg elevations are observed in pseudopheochromocytoma [9]. A more distinguishing feature is that panic attacks are
preceded by intense fear and panic. In contrast, in paroxysms of pseudopheochromocytoma, anxiety, if present, is provoked secondarily by the symptoms [10]. In the case of our patient, anxiety did not precede the paroxysmal hypertensive episodes.

With the exclusion of these possibilities, pseudopheochromocytoma was explored as a diagnosis. Pseudopheochromocytoma is a condition more common in women, characterized by unexplained paroxysmal hypertensive episodes accompanied by symptoms suggestive of a pheochromocytoma, such as chest pain, palpitations, shortness of breath, lightheadedness, headache, and nausea. Patients may also report flushing, which is present in the majority of cases of pseudopheochromocytoma but absent in pheochromocytoma [11]. The frequency of episodes can range from once a day to less than once a month, and the duration of episodes varies from less than 10 minutes to 2 days [12]. Despite similarities to pheochromocytoma, biochemical and imaging studies in pseudopheochromocytoma fail to reveal abnormalities responsible for these symptoms.

Although pseudopheochromocytoma remains a diagnosis of exclusion, previous studies have described a few defining clinical features, all of which were present in our patient [9]. First, paroxysms occur spontaneously without an identifiable precipitating factor or emotional trigger. Further, patients often have a history of abuse or trauma or are described as having a “very even-keeled” personality [9,13] — elements that were evident in our patient. Finally, blood pressure elevation is accompanied by physical symptoms, which we previously described. A novel feature of our case was that during one episode, the patient had sensorimotor deficits purely on the left side, concerning for a stroke. Head CT and MRI were both negative. While “weakness” has previously been described as a symptom [13], this is the first report describing lateralizing sensorimotor changes in pseudopheochromocytoma to our knowledge.

Studies on this topic are sparse, and the pathophysiology is yet unclear other than that it appears to have a psychosocial component. Studies aiming to biochemically profile pseudopheochromocytoma have yielded conflicting results on the baseline levels of plasma catecholamines, with one study reporting epinephrine levels above controls [14] and another reporting epinephrine and norepinephrine levels similar to controls [15]. Adrenoreceptor hypersensitivity has also been implicated in the pathophysiology, based on studies that showed exaggerated blood pressure changes in patients in response to drug-induced alterations in plasma norepinephrine levels or the Valsalva maneuver, and an attenuation of this disproportionate response with beta- and alpha1-blockers [14-16].

Regarding treatment, randomized controlled trials are lacking. However, treatment recommendations have been made based on case series and speculations of the underlying mechanisms of this condition [9,12,13,15]. For sudden elevations in blood pressure, rapid-acting antihypertensive drugs, such as intravenous labetalol or oral clonidine, and/or rapid-acting benzodiazepines are suggested. For prevention, a combination of alpha- and beta-blockade with attention to hypotension is recommended. The similarity of these episodes to panic attacks (without the preceding panic) has also led to the use of antidepressants, such as SSRIs and TCAs, with positive results. Psychotherapy may provide additional benefits in a willing patient.

CONCLUSION

We have described previously unreported findings of lateralizing sensorimotor deficits in a case of pseudopheochromocytoma. These changes, which occurred during a hypertensive episode, were seen in the absence of any radiologic evidence of stroke or hypertensive encephalopathy. Over the subsequent 1.5 weeks of hospitalization, the patient’s deficits improved and blood pressure stabilized with beta blockade. Pseudopheochromocytoma should be considered in patients with intermittent episodes of severe hypertension and symptoms of catecholamine excess in whom work-up for other causes are negative, especially if a social history of trauma or abuse is present.
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