A Case of Extreme Hemodynamic Lability and Hypocalcemia

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Abstract: An epinephrine-secreting pheochromocytoma can present with a confusing picture of hemodynamic lability with rapid fluctuations between hypo- and hypertension. They are challenging to manage and diagnose. We herein present the case of a 44-year-old patient who presented with extreme hemodynamic lability due to an epinephrine-secreting tumor. We discuss the initial management, diagnosis, and definitive therapy of this relatively rare type of pheochromocytoma.

Key Indexing Terms: Pheochromocytoma; Hypotension; Hypertension; Catecholamines; Magnetic resonance imaging. **[Am J Med Sci 2009;338(3):241–244.]**

The rare epinephrine-secreting pheochromocytoma may manifest as rapid cyclical hypo- and hypertension. A metabolic clue to this tumor is hypocalcemia, which is thought to result from the calcitonin-like effect of adrenomedullin to promote bone deposition of calcium. Initial management of hemodynamic lability requires use of short-acting medications to control hypo- and hypertension, when one sorts out the diagnosis. Documentation of inappropriate catecholamine production is diagnostic, whereas tumor localization is achieved with either computed tomography (CT) scan or magnetic resonance imaging (MRI). Once the patient is stabilized for a period of time, preoperative phenoxybenzamine administration is required before definitive treatment with surgical resection.

CASE PRESENTATION

A 44-year-old man was transferred from an outside emergency department to Yale-New Haven Hospital after initial presentation with nausea, vomiting, hemoptysis, and shortness of breath. Before his admission, he described having experienced episodes of nausea and headache of several minutes duration for the past 6 months. He had been diagnosed with ephedrine-induced cardiomyopathy and hypertension at age 39 years. Since this diagnosis, he denied any further use of ephedrine-containing medications but continued to purchase medications sold for muscle mass enhancement and sexual stimulants through the Internet.

Initial presentation to the emergency room was notable for blood pressure 110/69 mm Hg and heart rate 107 beats/min. Orthostasis was noted by an increase of heart rate to 138/min and a decrease of blood pressure to 66/33 mm Hg in the upright position. Additional pertinent findings were flat neck veins, tachycardia, and mild wheezing. The rest of the physical examination was unremarkable. Laboratory values were notable for an elevated serum creatinine concentration of 1.6 mg/dL (baseline 1.0 mg/dL) and a hematocrit of 64%. Initial serum calcium concentration was 8.5 mmol/L. Electrocardiogram revealed ST-segment elevations in the anterior leads. Three liters of normal saline was administered in the emergency department, and the patient was immediately taken to the cardiac catheterization laboratory.

Normal coronary arteries were noted, and the patient was transferred to the cardiac intensive care unit for observation after the procedure. Shortly after arriving to the floor, the patient developed severe hypertension (210/105 mm Hg, confirmed on multiple measurements). In addition, he rapidly developed respiratory failure, requiring intubation and mechanical ventilation. During the initial hypertensive episode, 2.5 mg metoprolol was administered intravenously with no effect. Twenty-five minutes into the hypertensive episode, the blood pressure suddenly fell abruptly to 30 mm Hg systolic. An arterial line was inserted, and the original tracings are shown in Figure 1. Cyclical hyper- and hypotension with systolic peaks of 210 mm Hg and plateaus of 30 mm Hg were noted. During the hypertensive episodes, tachycardia was predominant, whereas slowing of the heart rate was predominant during hypotensive episodes. A second arterial line was inserted, and manual blood pressures were recorded to confirm the accuracy of the severity of hemodynamic instability observed. A central venous pressure was transduced via an internal jugular vein catheter and found to be 1 to 3 cm H_2O. Initial management consisted of fluid bolus administration. In addition, different vasopressors including phenylephrine, vasopressin, and dopamine were infused during the hypotensive episodes with no effect.

Episodes of rapid supraventricular tachycardia occurred, requiring repeated electrical cardioversion. The diagnosis of pheochromocytoma was considered at the time, and serum normetanephrines and metanephrines, as well as urine norepinephrine, epinephrine, and catecholamines were sent. Administration of phenoxybenzamine was considered but thought to be contraindicated, given the severe hypotension following episodes of hypertension. During 2 subsequent hypotensive episodes, a complete loss of pulse was noted, requiring chest compressions to maintain circulation. Rapid cyclical hypo- and hypertension continued for 24 hours after initial admission to the cardiac intensive care unit. Hypotensive episodes were managed with repeated fluid bolus administrations. Serum calcium level dropped to 4.8 mmol/L, despite 2 g of intravenous calcium gluconate injection. A calcium gluconate drip was started, requiring rates of 400 mg/hr during the first 48 hours to maintain calcium concentration at 7.5 to 8.5 mmol/L.

Frequency and amplitude of the hyper- and hypotensive episodes continued but were less pronounced on the second day of hospitalization. Metyrosine was started at 250 mg every 6 hours to block the biosynthetic pathways of catecholamines. A noncontrast abdomen and pelvis CT scan was obtained, which revealed a large left adrenal mass, as shown in Figure 2.

Hemodynamics stabilized further with ongoing metyrosine treatment. The patient was extubated and transferred to

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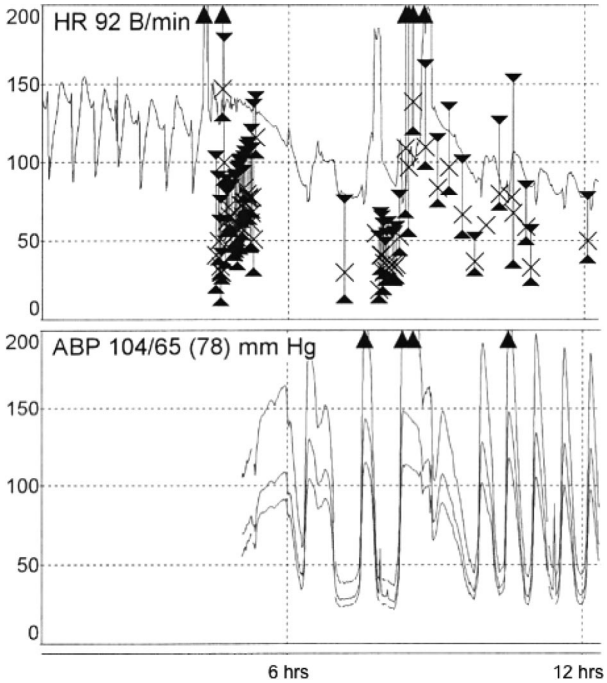

FIGURE 1. Recordings of the patient's blood pressure transduced via an arterial line and recordings of heart rate. Regular oscillations of the systolic blood pressure with peaks of 210 mm Hg and plateaus of 30 mm Hg, with 25-minute periodicity.

the floor on hospital day 5. Urine epinephrine levels obtained on hospital day 1 returned at 9080 μg (normal range, 0–20 μg/24 hr). In addition, metanephrine and normetanephrine levels were found to be elevated at 200 μg (normal range, $<$0.5 nmol/L for metanephrine and $<$0.9 nmol/L for normetanephrine). A repeat collection on hospital day 7 showed persistently elevated urine epinephrine at 200 μg with normal norepinephrine levels. On hospital day 10, the patient was discharged.

He was readmitted 6 weeks later, and an uncomplicated laparoscopic adrenalectomy (Figure 3) was performed successfully. Histopathologic examination showed diffuse pattern of growth with prominent spindling, focal atypia, and hyperchromasia. Tumor cells stained positively for multiple neuroendocrine markers including synaptophysin, chromogranin, and S-100 (Figure 4) consistent with pheochromocytoma.

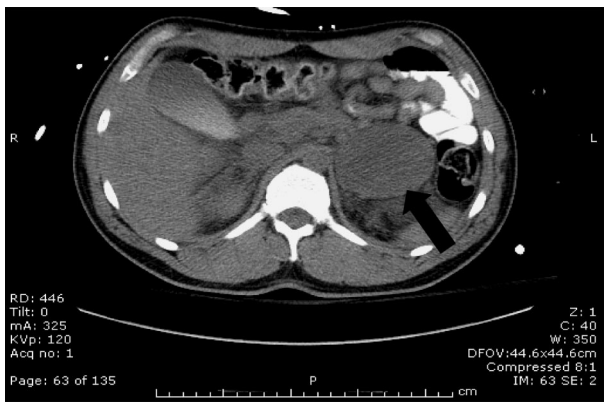

FIGURE 2. Computed tomography scan of abdomen and pelvis without contrast reveals 7.5 $\times$ 6 cm round mass (arrow) anterior and superior to the left kidney most consistent with pheochromocytoma.

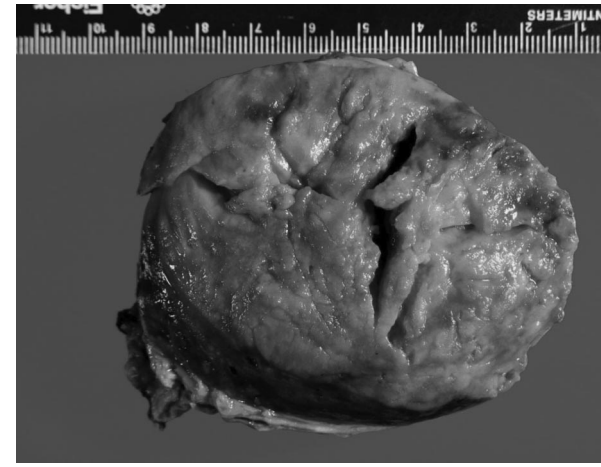

FIGURE 3. Laparoscopic adrenalectomy reveals 8 $\times$ 7 $\times$ 3.8 cm and 125 g encapsulated tan-pink soft tissue mass.

CLINICAL DIAGNOSIS

The case presented is a rare presentation of an epinephrine-secreting pheochromocytoma. These are neuroendocrine tumors that originate from catecholamine-producing chromaffin cells of the adrenal medulla or extraadrenal paraganglia. The clinical presentation is highly variable, and common symptoms are due to the direct actions of secreted catecholamines: hypertension, tachycardia, headache, pallor, and a feeling of panic or

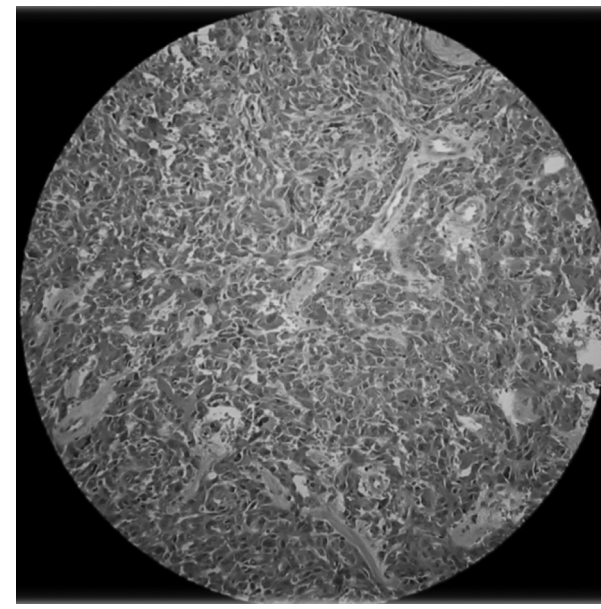

FIGURE 4. Histological confirmation of pheochromocytoma. Hematoxylin and eosin stain demonstrates a diffuse pattern of growth with prominent spindling. There is focal atypia and hyperchromasia with rare giant cells. Tumor cells stained positively for multiple neuroendocrine markers including synaptophysin, chromogranin, and S-100.