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MINI-FOCUS ISSUE: HEART FAILURE

BEGINNER

CASE REPORT: CLINICAL CASE

Hypersecretory Paraganglioma Presenting as Acute Aortic Dissection

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ABSTRACT

Abrupt, transient, and severe hypertension evoked by catecholamine-secreting tumors has the potential to manifest as acute aortic dissection. We report the successful, multidisciplinary management of an insidious, extra-adrenal, functional paraganglioma, suddenly presenting as acute aortic dissection. (**Level of Difficulty: Beginner.**)

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A 32-year-old man presented with acute substernal chest pain that radiated into the neck and had persisted over 48 h. He described severe, pressure-like pain slightly mitigated by ibuprofen. Ensuing dyspnea and diaphoresis prompted presentation to the emergency department. He reported associated intermittent headaches and generalized weakness. He disclosed smoking tobacco and drinking alcohol socially but denied illicit drug use. Family history identified early-onset hypertension in both parents. On arrival, blood pressure (BP) was 197/121 mm Hg with a heart rate (HR) of 86 beats/min. Physical examination demonstrated acute distress secondary to chest pain. Cardiopulmonary examination revealed a regular rate and rhythm without murmurs, rubs, or gallops and clear lungs. Abdominal examination exhibited no palpable masses. Distal pulses were 2+ throughout.

LEARNING OBJECTIVES

- To recognize and adequately triage chest pain representing AoD.
- To acknowledge a comprehensive diagnostic work-up of secondary hypertension.
- To distinguish between PCCs and PGLs.
- To recognize critical pharmacological and surgical strategy in functional PGL-induced AoD.

PAST MEDICAL HISTORY

Past medical history includes only hypertension. An unknown antihypertensive medication was initiated 2 years prior but had elapsed several months ago.

DIFFERENTIAL DIAGNOSIS

Acute-onset, severe chest pain with associated dyspnea is especially concerning for life-threatening conditions including acute coronary syndrome, acute aortic dissection (AoD), pulmonary embolism, tension pneumothorax, esophageal rupture, and cardiac tamponade. Markedly elevated BP at his age raised concern for secondary hypertension. Severe

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pain alone could have elevated BP, but this should not have been the only suspected cause. Major causes of secondary hypertension include medications (nonsteroidal anti-inflammatory drugs and so on), illicit drug use, chronic kidney disease, primary aldosteronism, hypercortisolism, pheochromocytoma, and functional paraganglioma.

INVESTIGATIONS

Blood chemistry revealed a creatinine level of 1.55 mg/dl (reference range, 0.55 to 1.02 mg/dl) without a baseline value for comparison. Electrocardiogram demonstrated left ventricular hypertrophy with diffusely inverted T-waves (**Figure 1**). Serial troponin draws had negative results. Urine toxicology detected tetrahydrocannabinol but not methamphetamines or cocaine. Chest x-ray displayed no effusions, pneumothorax, or mediastinal widening (**Figure 2**).

Computed tomography (CT) angiogram revealed a Stanford type A AoD involving the ascending thoracic aorta and aortic arch (**Figure 3**) with patency of the major aortic branch vessels. Due to surgical urgency, secondary hypertension work-up occurred after AoD repair and demonstrated normal serum aldosterone and renin activity. However, urine metanephrines and normetanephrines were elevated at 1,919 μg/24 h (reference range, 36 to 190 μg/24 h) and 12,352 μg/24 h (reference range, 35 to 482 μg/24 h), respectively. Free plasma metanephrines and normetanephrines were elevated at 494 pg/ml (reference range, <57 pg/ml) and 4,279 pg/ml (reference range, <148 pg/ml), respectively. Renal ultrasound revealed a hypoechoic mass adjacent to the left kidney. CT of the abdomen and pelvis confirmed a 5.8-cm left pararenal mass exhibiting an effect on the renal pelvis (**Figure 4**) with secondary left hydronephrosis.

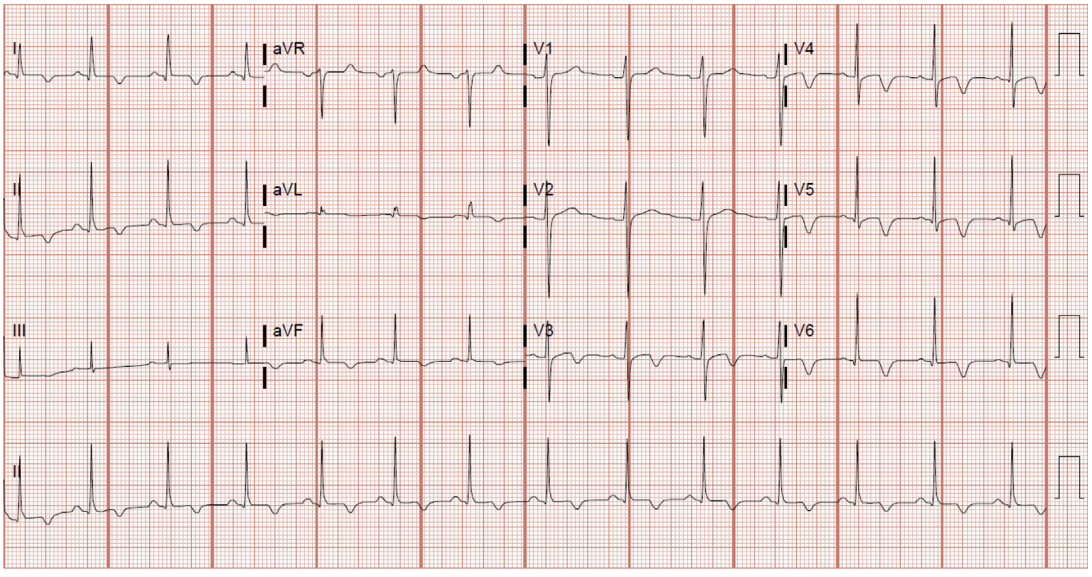
ABBREVIATIONS AND ACRONYMS

AoD = aortic dissection
BP = blood pressure
CT = computed tomography
HR = heart rate
PCC = pheochromocytoma
PGL = paraganglioma

MANAGEMENT

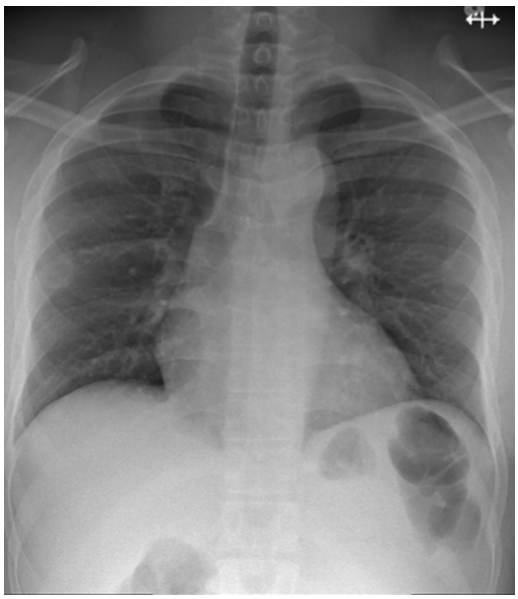
Clonidine and labetalol had mild success in controlling BP. Subsequent esmolol infusion was modestly effective. Because he showed no additional evidence of end-organ compromise, the patient was taken urgently for replacement of ascending aorta and underside of the transverse arch via cardiopulmonary bypass with deep hypothermic arrest and antegrade cerebral perfusion. Because intraoperative transesophageal echocardiogram showed no aortic insufficiency and only mild left ventricular hypertrophy, the procedure was limited to replacement of the ascending aorta, which included the site of intimal disruption. Hypertension persisted postoperative day 2, requiring high-dose clevidipine and nitroglycerin infusion. Eventually, BP was controlled, and secondary surgical

FIGURE 1 Electrocardiogram



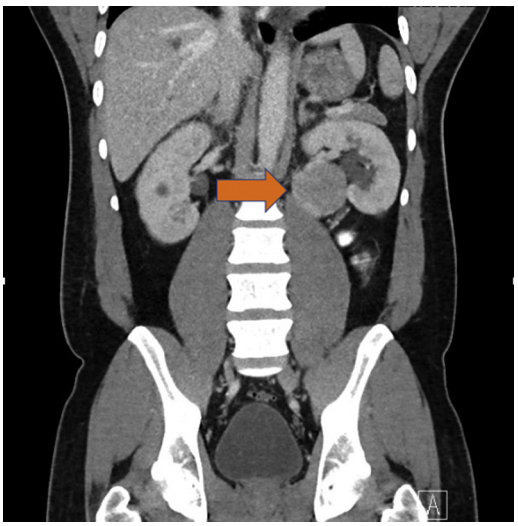
Electrocardiogram showing left ventricular hypertrophy with diffusely inverted T-waves.

FIGURE 2 Chest X-Ray



Chest radiograph demonstrating no acute cardiopulmonary process.

FIGURE 4 Computed Tomography of the Abdomen and Pelvis

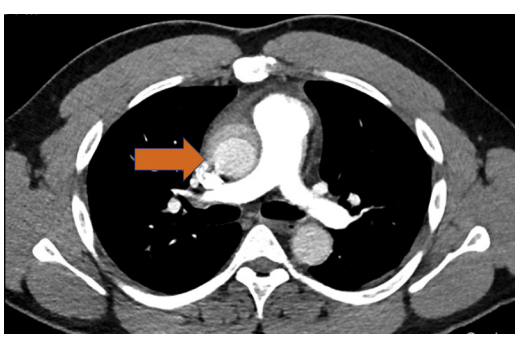


Computed tomography of the abdomen-pelvis revealing a 5.8-cm left pararenal mass **(orange arrow)**.

intervention was planned to address the suspected hypersecretory tumor. In addition to strategic adrenergic blockade with labetalol and doxazosin, the patient was discharged with amlodipine and lisinopril prescriptions on postoperative day 5.

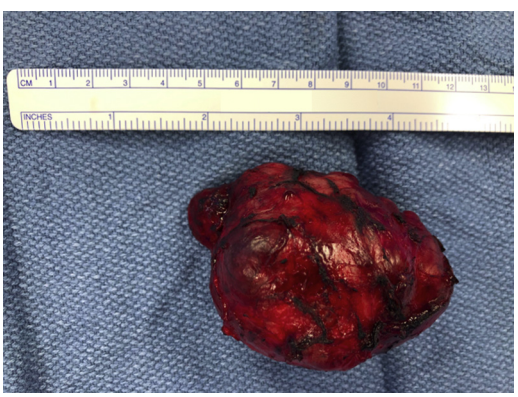
The patient returned in 6 weeks for tumor extraction. Mild BP elevation occurred during meticulous tumor resection. Post-resection hypotension did not occur. Open excision yielded a 72-g, grossly intact, tan, rubbery mass measuring 7.5 × 4.7 × 4.5 cm (Figure 5) immediately opposed to the renal vasculature. Repair of the renal vessels was required. Histological staining with hematoxylin and eosin revealed nests of bland spindle cells separated by thin trabeculae (Figure 6). Immunohistochemical stains yielded synaptophysin (neuroendocrine marker) with scattered cells displaying S100 proteins (embryonically derived from the neural crest) consistent with

FIGURE 3 Thorax Computed Tomography Angiography



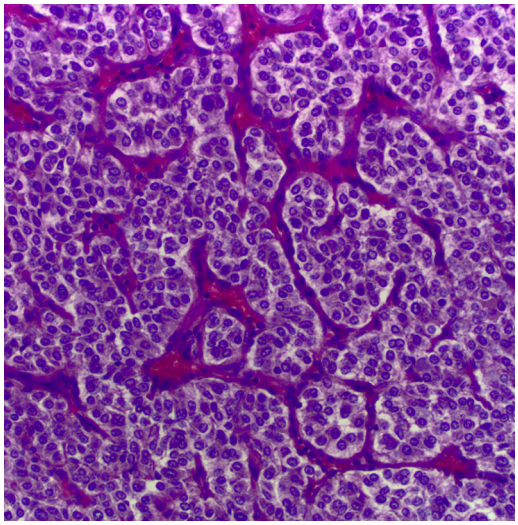
Computed tomography angiography revealing aortic dissection involving the ascending thoracic aorta **(orange arrow)**.

FIGURE 5 Gross Image of Paraganglioma



72-g, grossly intact, rubbery mass measuring 7.5 × 4.7 × 4.5 cm.

FIGURE 6 Pathology Slide of Paraganglioma



Zellballen pattern (small nests of polygonal/spindle-shaped cells in a rich vascular network) consistent with paraganglioma.

paraganglioma (PGL). Post-operative BP improvement was dramatic.

DISCUSSION

Stanford classification has established 2 categories for AoD: those involving the ascending aorta (type A) and those not (type B). Urgent and definitive imaging using transesophageal echocardiogram (preferred if hemodynamically unstable), CT, or magnetic resonance imaging is recommended. Initial management should decrease aortic wall stress by controlling HR and BP, limiting the extension of dissection. Intravenous beta-blockade is recommended and should be titrated to a HR ≤60 beats/min and systolic BP of 100 to 120 mm Hg. If systolic BP remains suboptimal, intravenous vasodilators (e.g., clevidipine and nitroglycerin) should be administered. Emergent surgical evaluation should be sought given the associated risk of life-threatening complications. Surgery, typically indicated for type A AoD, involves intimal tear excision, obliteration of the false lumen entry, reconstitution of the aorta with placement of a synthetic vascular graft, and repair or replacement of the aortic valve (1).

PGLs, present in about 0.1% to 0.6% of the hypertensive population, are neuroendocrine tumors arising from extra-adrenal autonomic paraganglia (2). They consist of neural crest-derived neuroendocrine cells with the potential to secrete catecholamines in abundance. PGLs are categorized as sympathetic or parasympathetic depending on paraganglia origination. Sympathetic PGLs, commonly located in sympathetic paravertebral ganglia of the thorax, abdomen, and pelvis, frequently are functional (catecholamine-secreting). Norepinephrine-secreting tumors usually cause sustained hypertension directly proportional to norepinephrine levels, whereas tumors that produce epinephrine co-secreted with norepinephrine typically produce paroxysmal hypertension. Symptoms can include headaches, sweating, palpitations, anxiety, tremors, pallor, and nausea. Histologically and functionally similar, a PGL that forms in the adrenal medulla is a pheochromocytoma (PCC) (2,3). Although rare, abrupt, transient, and severe hypertension evoked by intra-adrenal PCCs has manifested as AoD, but PGL-induced reports are extremely scarce (4). The current literature reveals annual incidence of both PCC/PGL (2 to 10 cases/million) and AoD (2 to 3.5 cases per 100,000 person-years) to be particularly rare (1,3). These 2 entities occurring together has only been reported a handful of times, typically in the form of PCC-induced AoD, however, to our knowledge, there has been only one other reported PGL-induced AoD (5). Surgical treatment of functional PGLs presents several challenges requiring multidisciplinary expertise and pre-operative planning. Secondary PGL extraction can produce intractable hypertensive crisis secondary to tumor manipulation (4). Pre-operative adrenergic blockade is essential prophylaxis for catecholamine release. In our case, PGL extraction was planned 6 weeks later to establish ample adrenergic blockade. Nevertheless, at least 10 to 14 days of blockade are recommended (4). Traditionally, PGLs are resected by means of open surgical procedures due to their multicentricity and close relationship with major vascular structures. PGLs can be highly vascular, especially in the head and neck, which should be considered during surgical excision. Once a functional PGL is removed, BP medications should be reassessed accordingly.

FOLLOW-UP

The patient tolerated both procedures very well. Once the PGL was removed, improvement in BP was significant, and he was eventually weaned off all antihypertensive medications. Plasma free metanephrines, drawn 8 weeks post-extraction normalized to 48 pg/ml (reference range, <57 pg/ml). His

acute kidney injury resolved, and he is able to work and exercises 3 days per week without limitation.

CONCLUSIONS

In summary, this case demonstrates a multifaceted diagnostic dilemma of important clinical significance. AoD risk posed by hypertensive emergencies is real, but occurrence is especially rare in the setting of a hypersecretory PGL. To our knowledge, this is the second reported case of this entity. Of critical importance is the allowance of ample duration between initial AoD repair and secondary PGL extraction for sufficient adrenergic prophylaxis prior to PGL manipulation. Moreover, this case describes a safe, strategic, and multidisciplinary approach to address 2 uniquely challenging cardiovascular events.

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