A CASE REPORT

Chronic Abdominal Pain: "The Great Masquerader"

by Deepa Shah, Janet Reiser

CASE PRESENTATION

A twenty-seven-year-old African American gentleman was evaluated for abdominal pain of seven years duration. The pain initially began when the patient was running quickly for exercise. Subsequently, it progressed such that walking precipitated abdominal pain. He had three previous episodes of bilious emesis without any prior history of peptic ulcer disease or associated abdominal pain. During the past year, he also had 10 pounds of unintentional weight loss. The patient denied hematemesis, melena, and hematochezia.

His medical history consisted of hypertension, diagnosed two years prior and treated with lisinopril and metoprolol, and asthma that was well controlled. He denied use of non-steroidal anti-inflammatory medications and had no drug allergies. His only prior surgery consisted of an anterior cruciate ligament repair of the left knee. Family history was negative for malignancy. Social history was positive for alcohol (6 drinks on weekends) and tobacco use (4 pack year history) and negative for drug use. His review of systems was positive for headaches, nausea, vomiting, anxiety, depression, chest pain, abdominal pain, and asthma. Physical examination revealed a normal blood pressure but he was tachycardic with a heart rate of 115. He had a thin and muscular abdomen that was soft, nontender and non-distended on exam; there was no hepatosplenomegaly and there were no hernias.

As part of the initial evaluation of his abdominal pain, esophagogastroduodenoscopy (EGD) was requested. Despite adequate sedation, the EGD was unable to be performed as the patient became very combative and agitated. As such, an upper GI with small bowel follow through (SBFT) was ordered; the findings were unremarkable. Routine labs including a complete blood count (CBC), complete metabolic panel (CMP), erythrocyte sedimentation rate (ESR), iron studies, thyroid stimulating hormone (TSH), cobalmin (B12), and *H. pylori* stool antigen were all normal or negative.

Transabdominal ultrasound revealed an oval,well-circumscribed mass along the anterior margin of the aorta in the retroperitoneum that was contiguous with the head of the pancreas. Subsequent abdominal CT scan confirmed presence of a large (heterogeneous) intensely enhancing mass in the retroperitoneum measuring 5 × 3.8 × 5 cm. The lesion was situated in the area of the inferior vena cava, with possible compression of this vascular system. Differential diagnosis, based on imaging studies, included lymphoma, sarcoma, and angiosarcoma. Decision to pursue CT guided biopsy of the lesion was contemplated; however, after further discussion with a radiologist, a new diagnosis of pheochromocytoma was postulated. As pheochromocytomas are highly vascular, the biopsy was cancelled because of concern for increased risk of bleeding. Laboratory markers (Table 1) confirmed the diagnosis of pheochromocytoma.

Once the diagnosis of pheochromocytoma was confirmed, Multiple Endocrine Neoplasia (MEN) 2a syndrome was excluded with normal intact parathyroid home (PTH) and calcitonin levels. Positron emission tomography (PET) computed tomography (CT) revealed significant fluorodeoxyglucose (FDG) activity limited to the retroperitoneal mass without metastases. Although the high FDG activity was suspicious for malignancy, the lack of metastases favored a diagnosis of benign pheochromocytoma.

A hematology oncology consultation was obtained and further patient history was elucidated. It was discovered that the patient's mother had a pheochromocytoma that was resected when she was 25 years-old, thus his

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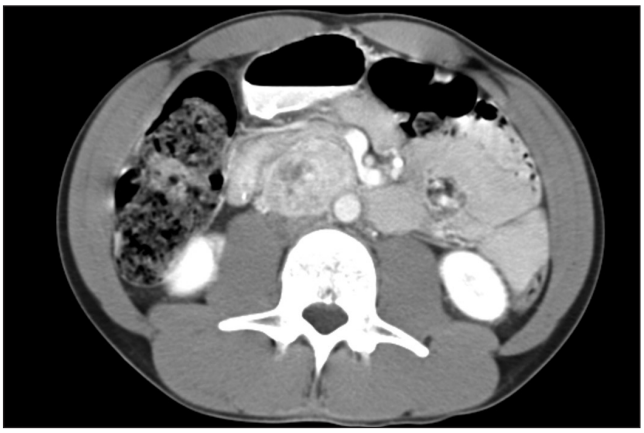

Figure 1. CT Image of mass.

diagnosis was consistent with hereditary pheochromocytoma. Surgical removal of the tumor was suggested for cure. Two weeks prior to surgical resection of the mass, alpha blockade (prazosin 1 mg three times per day) was initiated while he remained on lisinopril and metoprolol. Successful surgical removal of a heme-filled 8 × 15 cm pulsatile mass was performed. The mass was overlying the vena cava and wrapped itself around infrarenal aorta, but it did not appear to be rising from vena cava. Intraoperatively, the pathologist confirmed the mass was indeed a pheochromocytoma. The patient tolerated the procedure without any complications, had a successful recovery, and no longer required antihypertensive medications post-operatively. Final pathology revealed an extra-adrenal neoplastic pheochromocytoma that was completely resected. There was no pathologic evidence of necrosis or smaller cell types that would be suggestive of a malignant pheochromocytoma. Metastases were not present in this case.

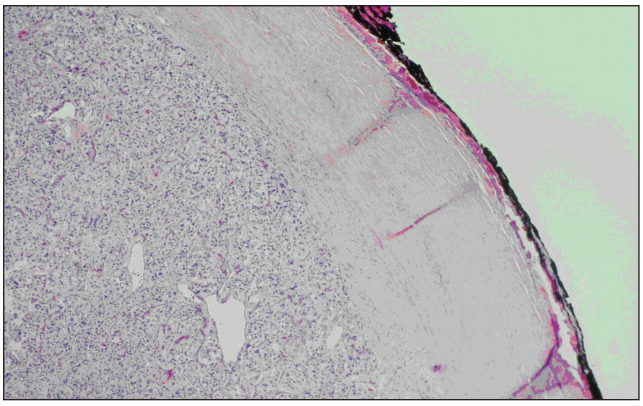

Figure 2. Gross Photo of specimen.

Table 1.
Laboratory Markers

- 24 HR urine normetanephrine: 4286 H (40–412) mcg/24 h
- Total metanephrines: 4381 H (94–604) mcg/24 h
- 24 HR norephinephrine: 1298 H (15–100) mcg/24 h
- Calculated total (e + ne): 1298 H (26–121) mcg/24 h
- 24 H dopamine: 1821 H (52–480) mcg/24 h
- 24 hr VMA: 19.7 H (nl <6) mg/24 h

DISCUSSION

Pheochromocytomas are catecholamine-producing tumors derived from the sympathetic or parasympathetic nervous system. These tumors may develop sporadically or be inherited with features of MEN type 2 or other pheochromocytoma-associated syndromes (1). Pheochromocytoma is a rare entity estimated to be found in 2–8 out of 1 million persons per year (1), and approximately 0.1% of hypertensive patients have a pheochromocytoma (2–4). Mean age at diagnosis for sporadic pheochromocytoma is 40 years, however hereditary forms are usually diagnosed earlier (5–7). The "rule of tens" for pheochromocytoma states that 10% are bilateral, 10% are extra-adrenal, 10% are familial, and 10% are malignant (8).

Clinical presentation of pheochromocytoma can vary greatly, and thus it has been termed "the great masquerader". The classic symptoms consist of palpitations, headaches, and profuse sweating. The presence of these three symptoms, in conjunction with hypertension, is highly suggestive of the diagnosis of pheochromocytoma (1). Pheochromocytomas can present with abdominal pain as the only symptom; however most of time these patients have acute abdominal pain (9–11). Various etiologies for acute abdominal pain attributed to the pheochromocytoma have been reported: spontaneous rupture (12–15), trauma (16), hemorrhage (17–21), ischemic colitis (22,23), release of vasoactive peptides (24), and bowel perforation (25,26). Review of the literature indicates that chronic abdominal pain is a relatively uncommon presentation of pheochromocytoma, with only a few cases reported (27–30). Paroxysmal signs and symptoms, secondary to episodic secretion of catecholamines, can often be a clue to aid in the diagnosis of pheochromocytoma. Anesthesia is a well-

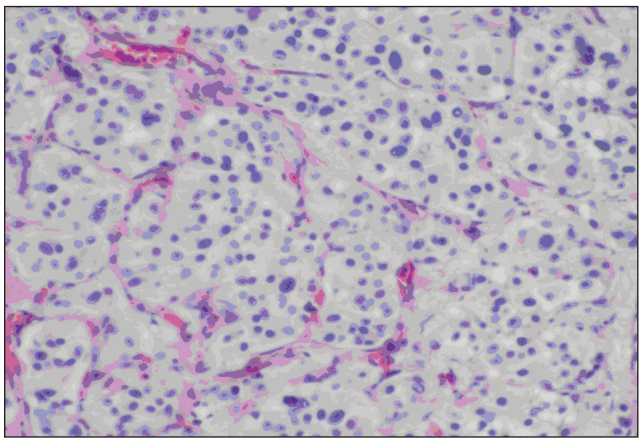

Figure 3. Microscopic pathology. Mass composed of neoplastic cells in alveolar or nested "zellballen pattern" with fibrous septa surrounding these cells.

known stimulus to elicit a catecholaminergic crisis, and perhaps this patient's reaction to sedation for his EGD was secondary to his underlying diagnosis (7,31,32).

Elevated urinary and plasma cathecholamines, metanephrines (normetanephrine and metanephrine), and vanillymandelic acid (VMA) are essential for confirming diagnosis of this condition (1). Among these tests, the fractionated metanephrines and catecholamines are 98% sensitive and specific (33). CT scan of the abdomen and pelvis with and without contrast is the initial imaging modality for localization of adrenal or possible extra-adrenal pheochromocytomas (1). In the above case, there was a discrepancy between the CT estimated size of the mass and the surgical specimen, which can be explained by differences in measurement with CT (anterio-posterior and transverse diameters) and surgical specimens (longitudinally using the longest dimension). Furthermore, once the mass was resected it was no longer compressed by surrounding bodily structures. T2-weighted Magnetic Resonance Imaging (MRI) with gadolinium enhancement has a similar diagnostic sensitivity to CT scanning, but it is preferred for localization of extra-adrenal tumors or tumors during pregnancy (34–35). CT and MRI are 70–80% specific for detection of pheochromocytoma, and enhanced mass identification can be achieved by ^{123}I-metaiodobenzylguanidine (MIBG) scanning (specificity 95–100%) (36–37). This imaging modality is most relevant in patients with extra-adrenal or large (>5 cm) adrenal tumors with increased risk of malignant disease, or in patients with high suspicion of multifocal disease (38). ^{18}F-fluorine PET has better diagnostic sensitivity than ^{131}I-MIBG scintigraphy, especially in metastatic pheochromocytomas where the compound can localize more foci than the ^{131}I-MIBG (39,40). In the above case, the lack of metastases on PET scan supported a benign lesion, but the mass itself was concerning for malignancy by PET criteria. This serves as a reminder to clinicians that PET scans can be falsely positive in a metabolically active tumor. Although it can be difficult to distinguish benign versus malignant pheochromocytoma, the presence of metastasis into nonchromatin tissue is confirmatory for malignancy (41).

Complete tumor removal is the ultimate therapeutic goal. Preoperative alpha blockade is essential to prevent catecholamine induced, serious, and potentially life-threatening complications during surgery (42–44). Traditional medications include phenoxybenzamine, prazosin, doxazosin, or urapidil, as these all assist with alpha blockade. Phenoxybenzamine is often preferred because it blocks alpha receptors non-competitively. Other alternative medications that can be used alone or in combination with alpha blockers include labetalol or calcium-channel blockers (dihydropyridines) (1). Surgery should be performed by anesthesiologists and surgeons who are experienced in the management of pheochromocytomas. Although laparotomy was the traditional surgical approach, laparoscopy (either transperitoneal or retroperitoneal) is the preferred method, as it is associated with fewer complications and expedited recovery (45). Postoperatively, it is important to document catecholamine normalization (1).

CONCLUSION

A multidisciplinary approach to diagnosing and treating pheochromocytoma is imperative to patient care, especially as illustrated by this case in which two other specialists were able to assist with the diagnosis. The radiologist was able to integrate the clinical presentation with radiological imaging, and thus prevented an unnecessary biopsy of a potentially highly vascular lesion. The hematologist-oncologist elicited positive family history of pheochromocytoma, which aided in the final diagnosis of hereditary pheochromocytoma.

Hypertension in a young person (under age 30) deserves secondary work-up for other etiologies.

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Pheochromocytoma, although unusual, should be considered in the differential diagnosis for chronic abdominal pain, especially if a patient also has concurrent palpitations, sweating, and headaches. If suspicious of this etiology, one should be cautious with anesthesia, as it can often cause a paroxysmal reaction related to catecholamine surge. Pheochromocytomas are highly vascular and should not be biopsied. Although they can have malignant appearance on CT scan, the only reliable predictor of malignancy is metastasis. Recognition of pheochromocytoma is essential because cure is potentially achievable through surgery. ■

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