When is a carcinoid not what it seems?

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Abstract

Paragangliomas and pheochromocytomas are unusual tumors with a distinct clinical and biochemical profile. The hallmark of these tumors, which are derived from chromaffin cells, is secretion of catecholamines causing hypertension and other symptoms of catecholamine excess. We report a tumor which presented in lung parenchyma, appearing as a low grade carcinoid tumor, but which exhibited the clinical profile of a pheochromocytoma. The patient did well with surgical treatment only and is alive today ten years after presentation, free of disease.

Keywords: Pheochromocytomas, carcinoid tumor, paraganglioma, chromaffin

Introduction

Pheochromocytoma is a difficult entity to diagnose, even when it occurs within the adrenal glands; however, when extra-adrenal pheochromocytomas do arise, it is often hard to label them as such. Pheochromocytomas are most often recognized due to elevated levels of catecholamines in blood/urine samples and computerized tomography (CAT) scans revealing that a mass exists. Pheochromocytomas are usually associated with headaches, sweating, palpitations and most often hypertension [1-3].

Low grade carcinoid tumors are not often associated with malignant hypertension. They can be found anywhere in the body, but most commonly in the small bowel, lung, or pancreas. Some are non-secretory, but many secrete active hormones. Most famously, those afflicted with the carcinoid syndrome may have transient hypertension, not the type usually associated with pheochromocytomas.

Case presentation

The patient, at the age of 53, was admitted to the hospital after complaining of shortness of breath and was in respiratory arrest when she arrived. She suffered from Type II adult onset diabetes mellitus, chronic obstructive pulmonary disease (COPD), and a 40-pack-year history of smoking. At the time, she was found to have pulmonary edema and cardiomyopathy. She was intubated, pulseless, and had a hypertensive crisis with a maximal blood pressure of 240/120 mm Hg as she was being revived. She had a 24-hour urine test with metanephrine concentration of 316 mcg, normetanephrines of 471 mcg, and total metanephrines of 831 mcg. She also had a 5-HIAA level of 12.5 over the same 24-hour period.

To make a diagnosis of a pheochromocytoma, one or more of the following must be true on 24-hour urine collections:
- Norepinephrine >170 mcg/24 hours
- Epinephrine >35 mcg/24 hours
- Dopamine >700 mcg/24 hours
- Norepinephrine >900 mcg/24 hours or metanephrine >400 mcg/24 hrs.

[measurement of plasma catecholamines is not accurate, and therefore not utilized].

She had a workup for a pheochromocytoma due to the high urinary vanillylmandelic acid (VMA) levels observed, but the tests were negative. A CAT scan revealed a 4.4x2.5 cm heterogeneous mass in the pulmonary hilum, abutting the descending thoracic aorta sitting approximately 3 cm from the carina. The patient underwent a biopsy and the mass had an absence of necrosis and presence of less than 2 mitoses per high power field (HPF); thus it was felt she had a low grade carcinoid tumor (Figures 1-4 and 5-10). Neither low power nor high power views were consistent with pheochromocytoma. It was decided that the mass should be removed. Intraoperatively, the mass was actually intraparenchymal and it involved both lobes. The mass could not be removed entirely without a pneumonect-
tomy; as a result, her entire left lung was removed. Pathology was consistent with a low grade neuroendocrine tumor.

**Discussion**
Both pheochromocytomas and paragangliomas secrete catecholamines and metanephrines. Extra-adrenal pheochromocytomas are difficult to diagnose. The high frequency of adenomas in normal adrenal glands can make CAT scans difficult to interpret. Extra-adrenal pheochromocytomas occur and can elevate systemic metanephrine levels, can cause hypertensive crises, tachycardia, or organ damage as a result of hypertensive crises. Due to the rarity of these tumors, however, they often go undiagnosed and/or misdiagnosed.

The tumors are often only diagnosed correctly after removal. The question becomes, then, can other patients, those with carcinoid tumors, present in a similar fashion to those with pheochromocytomas? That is, can they present with the same constellation of symptoms and the same biochemical profile? The answer, at least in this case, is yes.

Pheochromocytomas are most often initially seen on CAT scans. After identification, tumors can be removed with open or laparoscopic techniques. Prior to surgery, meticulous control of hypertension both alpha and beta blockade should be instituted. Long-term control of hypertension, even after the tumor is removed, is sometimes necessary. With antihypertensive treatment the patient can continue a normal life free of the many plaguing symptoms of the tumor.

Our patient had a pneumonectomy in 2002. She has been under constant surveillance and has had multiple CAT scans.
Figure 5. Immunostaining for NSE is negative (100X).

Figure 6. Immunostaining for EMA is negative (100X).

Figure 7. Positive staining is noted for synaptophysin (100X).

Figure 8. Positive staining for neurofilament (100X).

Figure 9. Negative staining is noted for AE1/AE3 (100X).

Figure 10. Negative staining is also noted for vimentin (100X).
since the operation. She is still receiving multiple antihypertensives, but with no evidence of recurrence. She is doing quite well. With no recurring hypertensive crises or elevated metanephrine levels the patient is likely cured. The patient’s tumor was histologically a low grade carcinoid, though it behaved as if it were a pheochromocytoma or paraganglioma with endocrine and cardiovascular near catastrophes.

A tumor’s presenting location can be deceptive. Our patient’s tumor appeared to be a low grade carcinoid originating in the lung, both by location and histologic appearance. However, with respect to clinical behavior (malignant hypertension, respiratory failure and cardiac arrest at presentation) and biochemical secretory signatures, we feel that this patient most likely suffered from an extramedullary pheochromocytoma.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions

| Authors’ contributions                  | RG | DG | CA |
|----------------------------------------|----|----|----|
| Research concept and design            | ✓  | ✓  | ✓  |
| Collection and/or assembly of data     | ✓  | ✓  | ✓  |
| Data analysis and interpretation       | ✓  | ✓  | ✓  |
| Writing the article                    | ✓  | ✓  | ✓  |
| Critical revision of the article       | ✓  | ✓  | ✓  |
| Final approval of article              | ✓  | ✓  | ✓  |
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