CLINICAL VIGNETTE

An Unusual Case of Mediastinal Paraganglioma Presenting as Bronchial Obstruction and Lung Collapse

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Introduction

Paragangliomas are neuroendocrine tumors that can occur in any location containing paraganglionic tissue. In adults, approximately 10% of paragangliomas arise from the chromaffin cells of the paraganglionic system in the bladder, cranium, thorax and abdomen, whereas 90% arise from the adrenal medulla.[1] Paragangliomas derive from either parasympathetic or sympathetic paraganglia. Those originating from parasympathetic paraganglia are usually located in the neck, skull base, and carotid body.[1] These are generally non-secretory (less than 5% of cases), and are frequently part of a genetic syndrome (over 50% of cases).[2] Conversely, paragangliomas originating from the sympathetic chain between the skull base and the bladder tend to exhibit excess catecholamine secretion (approximately 85% of cases) and are less commonly part of a genetic constellation of symptoms (less than 25%).[2] Paragangliomas are closely related to pheochromocytomas and are indistinguishable at the cellular level.

The malignant potential of paragangliomas is difficult to predict. Early diagnosis and management are important in preventing metastasis, or less commonly, serious sequelae from compressive and obstructive features. We describe a case of a patient diagnosed with a non-secretory paraganglioma of the posterior mediastinum with lung invasion who presented in respiratory distress with post obstructive pneumonia.

Case Report

A 79-year-old male with a history of heavy tobacco use (100 pack-year), chronic kidney disease complicated by secondary hyperparathyroidism, COPD, atrial fibrillation, and hypertension first noted worsening chronic cough productive of green sputum about one year prior to his acute presentation. These symptoms were thought to be due to his smoking and COPD. His hypertension was controlled on amlodipine and losartan. He denied any symptoms of flushing, palpitations, diarrhea, tremors, headache, diaphoresis or weight loss. He had no significant family history except for a brother with an unspecified bone cancer.

He presented to the emergency department, brought in by a friend. He was tachycardic, febrile, and hypotensive. He was in respiratory distress and was acidotic and hypoxic on arterial blood gas. He was emergently intubated and started on broad spectrum antibiotics. CT of the chest revealed an obstructive left lower lung lobe lesion, for which he underwent endobronchial biopsy. Pathology showed nested islands of tumor cells with a highly vascularized periphery. Histochemical staining was positive for synaptophysin, chromogranin A, neuron specific enolase, and S-100. Staining for TTF-1, CK 7, CK 20, TTF1, P40 and P60 were negative. These findings were consistent with paraganglioma. The patient was additionally found to be positive for West Nile virus. He had a rapid recovery and was soon extubated. He did not have any serious neurological or pulmonary sequelae and was discharged home with endocrinology, pulmonology, and surgery follow up scheduled.

Subsequent biochemical evaluation was performed to evaluate for excess catecholamine secretion. Plasma metanephrines were below detectable threshold (less than 25 pg/ml) and plasma normetanephrines were 197 pg/ml with normal being less than 148 pg/ml. Urine metanephrines were 178 mcg/24 hours and Urine normetanephrines were 414 mcg/24 hours, both within normal limits. This was repeated at a later date, again with normal values.

Further imaging was done to better characterize the paraganglioma over the course of the following year as follows.

Date	Imaging technique	Findings
July 2018	CT chest	6.3 x 4.3 cm posterior mediastinal mass encroaching on aorta and left bronchus. Incidental 1.5 cm R adrenal nodule
July 2018	FDG- PET	Intense uptake in mediastinal mass with SUV 57. No other abnormal uptake. Bilateral adrenal adenomas < 10 HU
March 2018	MRI Chest	Redemonstration of mass, now measuring 7.4 cm in largest dimension, partially cystic
December 2019	CT chest	Mass now measuring 8 cm in largest dimension. Stable bilateral adrenal nodules, < 3 cm

The patient was evaluated by surgery and was recommended to have surgical removal of the paraganglioma, which was expected to be curative. However, the patient declined further intervention as he remained without symptoms. He also declined genetic testing. His bilateral adrenal adenomas appear unrelated to his paraganglioma and were stable and benign on imaging. Functional workup is in process to assess for cortisol excess.

Discussion

Paragangliomas are derived from neural crest cells and can be found anywhere along the autonomic innervation from the skull base to the bladder. The majority originate in the adrenals (which are also known as pheochromocytomas). Extra-adrenal paragangliomas are in the minority, estimated at 10 - 30% of all paragangliomas.[3] These are most often found in the head and neck region. Only about 2% of paragangliomas are mediastinal, and the majority of these are in the anterior compartment.[4] Primary lung paragangliomas are very rare, cited at between 2 to 8 cases per million.[5] About 150 cases of mediastinal paragangliomas have been reported to date, which make up about 0.3% of all mediastinal tumors.[6]

Paragangliomas tend to be asymptomatic and non-secretory. They can sometimes present with typical sympathetic symptoms such as hypertension, palpitations, headache, sweating, or syncope. However, those in the thoracic and abdominal cavity often have more subtle symptoms related to their location and mass effect. These symptoms include back and chest pain, cough, dyspnea, nausea, vomiting, and upper GI bleeding. Our patient's only initial symptom was chronic productive cough that was confounded by his COPD and smoking. Thus, diagnostic workup was delayed until he presented acutely with pneumonia related in part to mass effect and lung obstruction from his growing paraganglioma.

The initial workup for paraganglioma should include biochemical testing of urinary or plasma catecholamines, even if the patient does not appear to be symptomatic. This should be followed with imaging by CT or MRI. If there is concern for metastasis, a DOTATATE scan or FDG PET scan should be performed. Biopsy should be done only after ruling out catecholamine excess.[1]

Generally, surgical treatment is recommended for paragangliomas as their histological features do not correlate to prognosis or malignant potential. About 10% of all paragangliomas are malignant, and can only be labeled as such after metastatic spread is identified. Prognosis is favorable for mediastinal paragangliomas treated with complete resection. A 1994 review article of 79 cases of mediastinal paragangliomas reported a 10-year survival of 84.9% with complete resection compared with only 50% in the biopsy -only and partial resection subgroup.[6] They can also be treated with radiation but tend to be relatively resistant.

As many as half of the cases of paraganglioma share a genetic basis and can be related to a number of hereditary conditions, including von Hippel-Lindau, neurofibromatosis type 1, Carney triad, multiple endocrine neoplasia types 2a and 2b, and SDHB, SDHC, and SDHD mutations. Genetic testing should be offered in cases with a positive family history or with history of bilateral, extra-adrenal, or multifocal pheochromocytoma, a positive genetic mutation as well as those tumors with negative SDHB staining.[1] Hereditary paragangliomas present on average 10 years earlier than sporadic paragangliomas, frequently in multiple locations.[2]

Conclusion

This case highlights an atypical presentation of paraganglioma manifesting as a posterior mediastinal mass that led to bronchial invasion and lung collapse. In this patient with a history of COPD and heavy tobacco use, paraganglioma was a very distant contender on his initial differential diagnosis for cough, and later, post obstructive pneumonia. It serves as a reminder that while paragangliomas are commonly characterized as catecholamine-secreting adrenal tumors, they can occur anywhere along the sympathetic and parasympathetic nervous system and present unexpectedly with minimal catecholamine secretion. They respond well to surgical resection and genetic testing should be considered to detect familial syndromes.

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