

CLINICAL VIGNETTE

A Rare Case of a Rapidly Growing Pulmonary Large Cell Neuroendocrine Carcinoma

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Introduction

Neuroendocrine tumors are a diverse family of malignancies that can occur in multiple organ systems, including the respiratory tract. In the pulmonary system, neuroendocrine cells secrete various critical neuropeptides. Rarely, neuroendocrine tumors are a source of pulmonary malignancy.¹ These tumors are a spectrum and can be divided into four immunohistological categories by the WHO, including typical carcinoids, atypical carcinoids, large cell neuroendocrine carcinoma (LCNEC), and small cell lung cancer (SCLC).² Despite its name, under 5% of neuroendocrine tumors actually produce symptoms or signs related to hormone production.³

Case Report

A 52-year-old female with a 10-pack year smoking history presented to her primary care physician with three weeks of new onset non-productive cough. It was associated with nausea, fatigue, non-bloody diarrhea, subjective fevers, and unintentional weight loss of 20 pounds over the preceding month. She had stopped smoking four months prior to the onset of her cough. Earlier that year, the patient had been hospitalized for orthostatic hypotension attributed to a thiazide diuretic that had been prescribed for hypertension. The medication was discontinued, yet she continued to have periodic episodes of symptomatic lightheadedness with positional change. Her medical history was also significant for major depressive disorder, asthma, and severe hidradenitis suppurativa requiring treatment with intravenous antibiotics and several skin grafts.

The patient was admitted to the hospital for treatment of pneumonia, and further work-up of consolidation in the left upper lobe and peripheral ground-glass opacities on CXR. Eleven months prior, chest radiograph for asthma exacerbation, showed no consolidation or mass. CT of the chest with intravenous demonstrated a new large mass within the left upper lobe, measuring 8.7 x 6.4 cm, with mediastinal invasion into the para-aortic spaces, left peribronchial and left interlobar spaces, and obliteration of the left upper lobe and lingula. There were also discrete left paratracheal and subcarinal lymph nodes suspicious for regional nodal involvement, a 2.0 x 1.2 cm nodule in the left upper lobe, and subcentimeter nodules throughout the right lung consistent with metastases. She was treated with intravenous antibiotics for her post obstructive pneumonia.

Endobronchial biopsy showed large, undifferentiated cell neuroendocrine carcinoma, with focal mucin positivity, supported by mucicarmine staining. Molecular pathology was negative for an EGFR or KRAS mutation, and negative for ALK rearrangement. Transcervical mediastinal lymph node dissection revealed 6 out of 21 total lymph nodes with tumor involvement. Nd:YAG laser resection of the endobronchial tumor was also performed. Bronchial washings were negative for malignancy. Chemotherapy was initiated with cisplatin and pemetrexed. Given rapid disease progression on CT after just two cycles, her regimen was changed to carboplatin and etoposide along with fractionated radiation therapy. The patient's clinical course, however, continued to markedly deteriorate, requiring repeated hospitalizations for neutropenic infections and hemoptysis. Her course was further complicated by severe left upper extremity pain secondary to tumor encasement of her left subclavian artery and occlusion of her left subclavian vein due to distention. Imaging also showed left internal jugular thrombosis. The patient developed an incomplete Horner's syndrome with left eye ptosis and the patient died secondary to septic shock and massive hemoptysis less than four months after diagnosis.

Discussion

Approximately 20% of bronchopulmonary tumors are considered neuroendocrine in origin, with the majority SCLC (~95%).⁴ SCLC's is rapidly progressive and carries a high mortality.⁵ On the other hand, LCNEC are rare, accounting for only 1% of diagnosed lung cancers, and are less well studied and characterized.⁶ Outside of SCLC, the natural history of neuroendocrine tumors has not been well described. Males predominate in LCNEC diagnoses, including one series with 95% male population. Heavy smoking has been associated with the LCNEC, similar to its histologically related lung malignancy, SCLC. LCNEC presentation is similar to the more common lung malignancies with neuroendocrine signs being rare.⁷ It is unclear if our patient's orthostatic symptoms were secondary to a vasodilatory neuroendocrine effect from the tumor or simple dehydration. LCNEC is defined as a non-SCLC with neuroendocrine histologic features, large cell size, polygonal cell shape, prominent nucleoli, positive staining for at least one neuroendocrine marker besides neuron-specific enolase such as chromogranin, CD56/NCAM, or synaptophysin.

sin, and a high nucleocytoplasmic ratio.⁸ The neuroendocrine tumors are known to be slower growing and portend over a 50% 5-year survival. There are almost no reports in the literature of rapidly growing LCNEC.⁹

This patient did not have significant medical history other than a long-term diagnosis of hidradenitis suppurativa. Although the diagnosis has been associated with increased rates of adenocarcinoma and squamous cell carcinoma, no specific link has been established with neuroendocrine tumors specifically.¹⁰

Conclusion

The case represents an unusually aggressive and difficult to manage presentation of an unusual and poorly characterized disease. While rapidly growing SCLCs are common, the rest of the neuroendocrine tumor family has not been reported to grow this quickly. This case differs from most cancer cases where recent normal imaging was available. We can appreciate the speed of LCNEC tumor progression given the normal chest radiograph one year from onset of her presenting symptoms and diagnosis of large obstructing masses on CT.

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