Case Report

Radiological interpretation of a small cell neuroendocrine cancer of the lung

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Abstract

Neuroendocrine tumors may develop throughout the human body with the majority being found in the gastrointestinal tract and bronchopulmonary system. Neuroendocrine tumors are classified according to the grade of biological aggressiveness (G1–G3) and the extent of differentiation (well-differentiated/ poorly-differentiated). The well-differentiated neoplasms comprise typical (G1) and atypical (G2) carcinoids. Large cell neuroendocrine carcinomas, as well as small cell carcinomas (G3), are poorly-differentiated. The identification and differentiation of atypical from typical carcinoids or large cell neuroendocrine carcinomas and small cell carcinomas are essential for treatment options and prognosis. Pulmonary neuroendocrine tumors are characterized according to the proportion of necrosis, the mitotic activity, palisading, rosette-like structure, trabecular pattern, and organoid nesting. These neuroendocrine tumors of the lung arise from Kulchitzky cells of the bronchial mucosa and comprise typical carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma (LCNEC), and small cell lung cancer (SCLC). Here is a case report of the 75-year-old male patient presented with complaints of a cough and sudden onset of breathlessness and weight. On Computed Tomography (CT) a large heterogeneous lesion noted in the left anterior mediastinum which was subjected to CT guided biopsy. On histopathology and immunohistochemistry, the tumor was confirmed as small cell neuroendocrine tumor.

Key words

Neuroendocrine tumor, Primary Neoplasm, Kulchitzky cells, Anterior Mediastinum Mass.

Introduction

Neuroendocrine tumors may develop throughout the human body with the majority being found in the gastrointestinal tract and bronchopulmonary system. Neuroendocrine tumors are classified according to the grade of biological aggressiveness (G1–G3) and the extent of differentiation (well-differentiated/ poorly-differentiated). The well-differentiated neoplasms comprise typical (G1) and atypical (G2) carcinoids. Large cell neuroendocrine carcinomas, as well as small cell carcinomas (G3), are poorly-differentiated. The identification and differentiation of atypical from typical carcinoids or large cell neuroendocrine carcinomas and small cell carcinomas are essential for treatment options and prognosis. Pulmonary neuroendocrine tumors are characterized according to the proportion of necrosis, the mitotic activity, palisading, rosette-like structure, trabecular pattern, and organoid nesting. These neuroendocrine tumors of the lung arise from Kulchitzky cells of the bronchial mucosa and comprise typical carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma (LCNEC), and small cell lung cancer (SCLC).

Case report

A 75-year-old male patient presented with complaints of a cough and sudden onset of breathlessness. History of hemoptysis for the last 15 days was noted which was red in color on gross examination. There was History of weight loss from the past 6 months. There was no history of fever, evening rise of temperature, headache nausea, and vomiting. The study period was between 2017-2018 in the Department of radiology and imaging sciences, Shri Sathya Sai Medical College and Research Institute.

Imaging Findings

Etiology

Although lung NETs are considered a distinct family of tumors with shared morphologic, ultrastructural, immunohistochemical, and molecular characteristics [1]. There is evidence to suggest that TCs and ACs are morphologically distinct from LCNECs and SCLCs [7]. Mechanisms for the development and progression of well-differentiated lung NETs are unclear [2]. Most TCs and ACs arise de novo, although they would be classified as carcinoid tumorlets if discovered when they measure 5 mm or less [3, 4]. However, some TCs and ACs develop in patients with diffuse idiopathic neuroendocrine cell hyperplasia (DIPNECH), a rare preneoplastic lesion characterized by the association of preinvasive hyperplasia of PNECs and neuroepithelial bodies in the respiratory epithelium and multiple carcinoid tumorlets [4, 8–11]. A recent study has proposed the presence of PNEC hyperplasia in at least three bronchioles associated with three or more tumorlets as the minimum pathologic criteria necessary to diagnose DIPNECH in pathologic specimens [4].

Molecular Biology

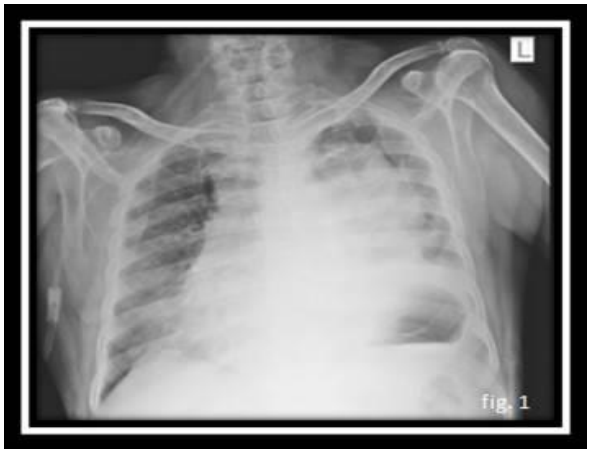
At the cellular level, LCNEC has a higher proliferative rate compared to LCC. A study from Ab'Saber, et al. [17] found that LCNEC had greater staining than LCC for p21waf1/cip1, which is involved in the regulation of apoptosis and the cell cycle, as well as microvessel density, a marker of angiogenesis. Patients found to have greater than 3.5% staining for p21waf1/cip1 and microvessel density staining of greater than 3.0% in their tumor specimens was found to be at high risk of death due to lung cancer [5].

On radiological work up

Chest radiograph demonstrated an ill-defined large radio-dense mass lesion involving the upper, middle and lower zones of the left lung with moderate left-sided pleural effusion. There is the elevation of the left hemidiaphragm with the collapse of the left lower lobe. On CT a large, irregular and round soft tissue density heterogeneous mass measuring 11.7×9.1×8.5cm is noted in the left anterior mediastinum, with posterior border of the mass appearing to abut the left main bronchus and left main pulmonary artery. A nodular lesion with HU value of 70 measuring 1.3×1.1cm is noted along the left oblique fissure suggestive of possible metastases. Few enlarged mediastinal lymph-nodes are

noted. Moderate left-sided pleural effusion with the massive collapse of the left lung is noted. Interlobar extension of pleural effusion into left oblique fissure is also noted. Mediastinum appears shifted to the left. Left hemi- diaphragm appears elevated. On MRI imaging a large mass lesion which appears heterogeneous with central areas of hypo-intensities on T2WI, hypo-intense on T1WI is noted in the left anterior mediastinum with moderate left-sided pleural effusion. CT guided biopsy was done which on histopathology analysis was suggestive of small cell neuroendocrine carcinomas of the lung (**Figure – 1 to 8**).

Figure - 1: Chest radiograph posterior-anterior view (PA) shows an ill-defined large radio-opaque mass lesion involving the upper, middle and lower zones of the left lung which is obscuring the left cardiac border as well as left hemi-diaphragm. There is moderate left side pleural effusion, tracheal deviation to the right side and elevation of left hemi-diaphragm.



Discussion

Neuroendocrine tumors of the lung rise up out of Kulchitzky cells that are frequently present in the bronchial mucosa and offer the fundamental morphologic features of neuroendocrine tumors including organoid settling, palisading, or rosettes [6]. These tumors address a wide clinical-pathologic range and have variable morphologic features and biologic practices [7]. In 2000, Garcia-Yuste et al proposed another portrayal of pneumonic neuroendocrine tumors that consolidates ordinary carcinoid, which is a low-quality risk; atypical carcinoid, which is a mid-run survey peril; and large cell neuroendocrine carcinoma (LCNEC) and little cell lung development (SCLC), which are high-audit malignancies [8]. These tumors speak to over 25% of each aspiratory neoplasm, in addition, the predominant piece of neuroendocrine tumors are SCLCs [9]. Treatment is dependent on the histologic features, which reflect differentiates in clinical direct and conjecture.

Figure - 2: Plain CT chest mediastinal window axial view shows a large, irregular, soft tissue density heterogeneous mass lesion measuring 11.7×9.1×8.5 cm in the left anterior mediastinum, with the posterior border of the mass appearing to abut the left main bronchus and left main pulmonary artery. The mass causes significant mediastinal shift to the right side.

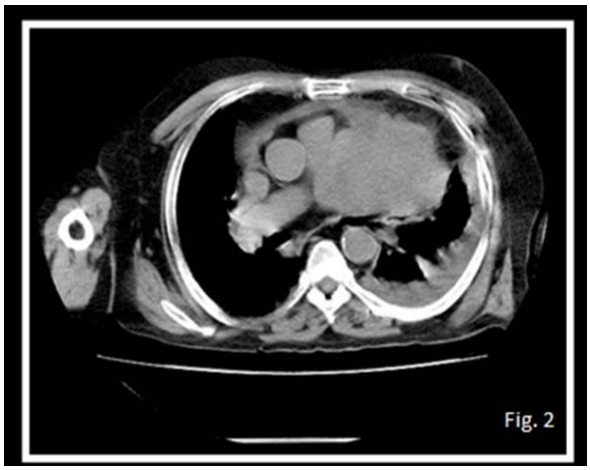


Figure - 3: Plain CT chest mediastinal window axial view shows a nodular lesion measuring 1.3×1.1cm along with the left oblique fissure.

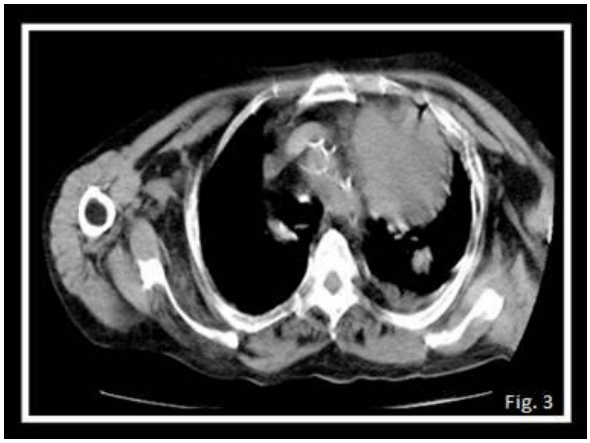


Figure - 4: Plain CT chest mediastinal window axial view shows moderate left sided pleural effusion with passive collapse of the left lung.

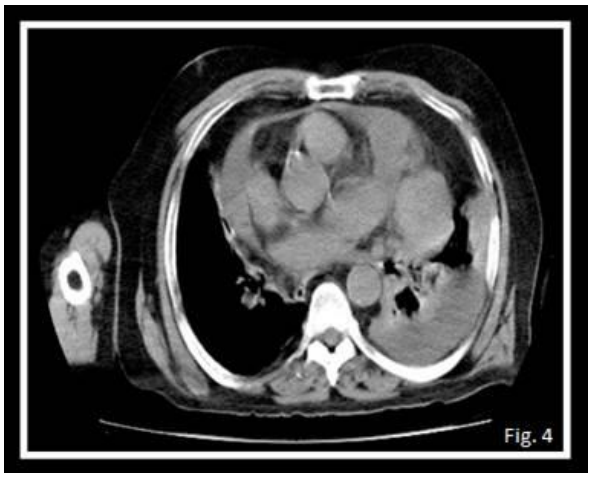


Figure - 5: Plain CT chest mediastinal window axial view shows CT guided biopsy acquired from lung lesion.

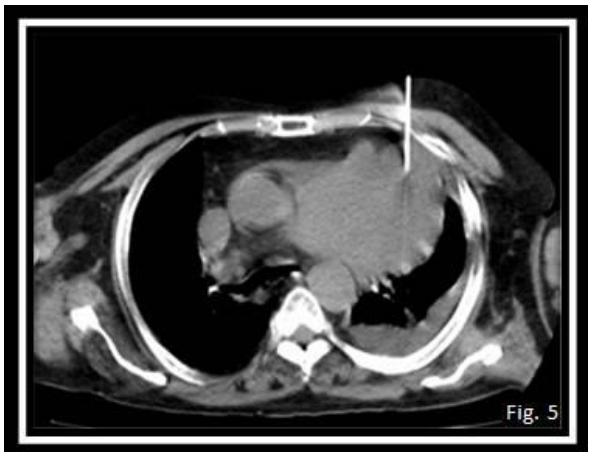


Figure - 6: Non-contrast T1WI MRI chest axial view shows a mass with hypo-intense signals in left anterior mediastinum and left sided pleural effusion.

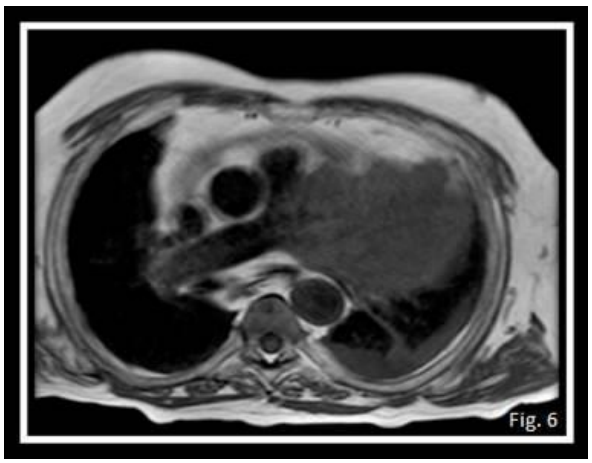


Figure - 7: Non-contrast T2WI MRI chest axial view showing a mass with heterogeneous signal intensity in the left anterior mediastinum with central areas of hypo-intensities. The posterior border of the mass appears to abut the left main bronchus and left main pulmonary artery. Mass causes significant mediastinal shift to the right side.

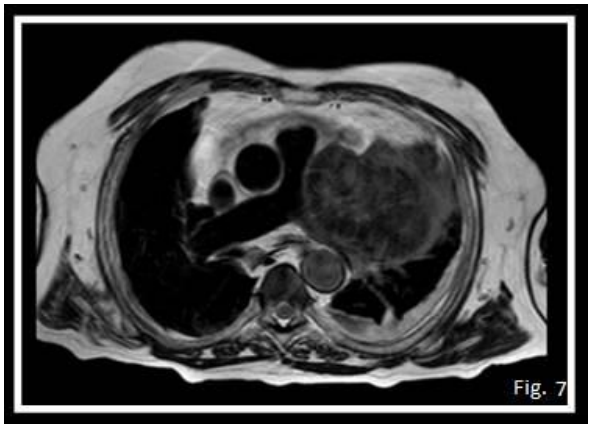
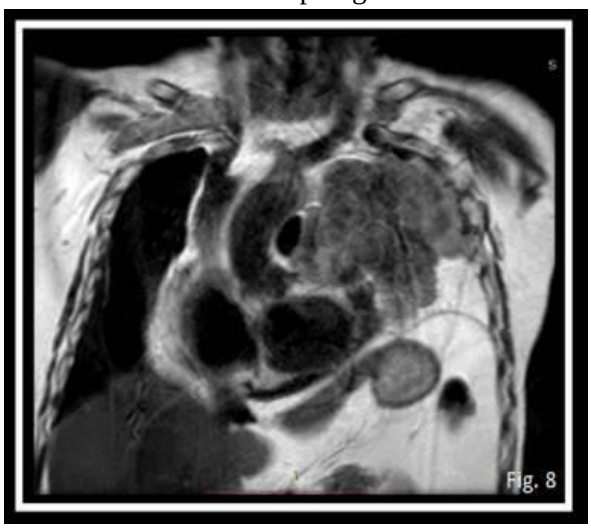


Figure - 8: Non-contrast T2WI MRI chest coronal view shows a hetero-intense mass is noted in left anterior mediastinum and there is elevation of left hemi diaphragm.



Small Cell Lung Cancer

Small cell lung tumor (SCLC) (also known as oat-cell lung malignancy) is a type of bronchogenic carcinoma. SCLC is different from non-small cell lung growth (NSCLC). SCLC has a unique presentation, imaging appearances, treatment, and prognosis. SCLCs are neuroendocrine tumors of the lung that quickly develop, are profoundly threatening, generally,

metastasize, and, in spite of demonstrating reaction initial response to chemotherapy and radiotherapy, have a poor prognosis and are typically unresectable [50]. Up to 15-20% of lung cancers present as small cell lung malignancies and are connected with cigarette smoking. It arises from the bronchial mucosa. Invasion of peri-bronchial connective tissue also occurs if local invasion into the submucosa. Cells are Small, oval, with scant cytoplasm and a high mitotic count [11]. Common clinical signs are dyspnea, a persevering hack, hemoptysis, and post-obstructive pneumonia. SCLC is usually present with necrosis within, superior vena cava (SVC) invasion/SVC obstruction, and paraneoplastic disorders. The invasion of surrounding structures may cause difficulties in swallowing, hoarseness of voice, and superior vena cava syndrome [12]. At the time of diagnosis, patients usually have an extensive disease with rapid tumor growth. Most cases will exhibit in advanced stages, not operable, and with a dismal prognosis. Just around 5% of patients present at the beginning (Ia, Ib, or IIa), with the effectively curable disease [13, 14]. Management include an aggressive chemo-radiation treatment and, some cases, with lobectomy related with mediastinal lymph dissection [Surgical excision is normally not suggested beyond these early stages, as studies have demonstrated that any nodal contribution (N1– 3 ailment) won't profit by the excisional treatment [15]. Brain metastases are found in up to a quarter of patients at presentation and is known as a common site of disease recurrence after an initial treatment response. Prophylactic cerebral irradiation (PCI) can be given for those with adequate systemic control and without metastases to the CNS [16, 17]. Advanced disease (stage IV) is managed only with chemotherapy aiming for palliation and symptoms control.

Conclusion

Neuroendocrine tumors of the lung originate from the Kulchitzky cells that are normally present in the bronchial mucosa SCLCs are the most rapidly progressing neuroendocrine pulmonary tumor and have the most specific imaging features like hilar or mediastinal lymphadenopathy. Even though there are few overlapping with help of the clinical and imaging features of typical carcinoid, atypical carcinoid, LCNEC, and SCLC may be useful in differentiation of neuroendocrine pulmonary tumors and for further assessment and treatment.

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