CHAPTER 66

NEUROENDOCRINE TUMORS OF LUNG

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INTRODUCTION

Lung neuroendocrine tumors are a rare group of pulmonary neoplasms that undergo neuroendocrine differentiation and progress slowly.The origin of neuroendocrine neoplasms and tumor development is controversial. These tumors are thought to arise from Kulchitzky cells (or enterochromaffin cells normally found in the bronchial mucosa).Approximately 20-25% of all invasive lung malignancies consist of neuroendocrine tumors.(1-3)

Neuroendocrine tumors, which were first described as carcinoid tumors by Siegfried Oberndorfer in 1904, developed from endocrine cells. These tumors also have neuron-like properties. For this reason, they are called neuroendocrine tumors. However, 60% of these tumors are functionally active (there is hormone production). It is examined in three main sections according to the World Health Organization (WHO) 2015 classification:Carcinoid tumors (typical (TC) / atypical (AC)),Large cell neuroendocrine carcinomas (LCNEC),Small cell carcinomas (SCLC). (Table 1)(4,5)

Table 1.2015 WHO criteria for the diagnosis of pulmonary neuroendocrine tumors

Tumor type	Criteria
Typical carcinoid	Carcinoid morphology and <2 mitoses/2 mm2 (10 HPFs), lacking necrosis and >0.5 cm
Atypical carcinoid	Carcinoid morphology with 2 to 10 mitoses/2 mm2 (10 HPFs) or necrosis (often punctuate)
Large cell neuroendocrine carcinoma	Neuroendocrine morphology (organoid nesting palisading rosettes, trabeculae); High mitotic rate >10/2 mm2 (10 HPFs), median of 70/2 mm2; Necrosis (often large zones); Cytologic features of a NSCLC: large cell size, low nuclear to cytoplasmic ratio, vesicular or fine chromatin, and/or frequent nucleoli; some tumors have fine nuclear chromatin and lack nucleoli but qualify as NSCLC because of large cell size and abundant cytoplasm; andPositive immunohistochemical staining for one or more NE markers (other than neuron-specific enolase) and/or NE granules by electron microscopy
Small cell neuroendocrine carcinoma	Small size (generally less than the diameter of three resting lymphocytes); Scant cytoplasm;Nuclei: finely granular nuclear chromatin, absent or faint nucleoli; High mitotic rate: >11 mitoses/2 mm2 (10 HPFs), median of 80/2 mm2 (10 HPFs); andFrequent necrosis, often in large zones

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the time of diagnosis, and 1 and 3-year survival rates were reported as 86% and 67%, respectively. In the study of Daddi et al., Age, smoking history and lymph node involvement were found to be statistically significant prognostic factors in multivariate analyzes in 247 AC cases.(30,37)

It has been reported that LCNECs are biologically aggressive like SCLCs, have a worse prognosis than other SCLCs, and their 5-year average survival is between 13-57%. Tumor recurrence and distant metastases develop rapidly despite complete resection even in the early stages. Iyoda et al., For all stages, reported the 5-year survival as 35.5% and the 5-year disease-free survival rate as 27.4%, and stated that the majority of relapses developed within the first 2 years. Although there are no specific prognostic and predictive markers due to the limited number of cases, it has been interpreted that LCNECs are tumors with poor prognosis, where all three markers, CD56 / chromogranin A / synaptophysin, are not positive. (38,39)

The average survival rate in SCLCs is 12.7 months, the 2-year survival rate in metastatic disease is 10%, and the 5-year survival rate in non-metastatic disease is approximately 25%. Advanced disease, poor performance status, weight loss, excessive amount of disease-related markers (eg high LDH) are poor prognostic factors. Young age, good performance status, normal creatinine level, normal LDH, single metastatic site were found to be associated with good prognosis in studies.(25,27)

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