Bronchial and Thymic Carcinoid Tumors

Anya Litvak, MD[a], M. Catherine Pietanza, MD[b,*]

KEYWORDS

• Bronchial • Thymic • Neuroendocrine • Typical carcinoid • Atypical carcinoid

KEY POINTS

- Bronchial carcinoids are well-differentiated neuroendocrine tumors that account for approximately 2% of all lung tumors.
- Bronchial carcinoids are usually sporadic, but may be associated with multiple endocrine neoplasia type 1 (MEN-1) syndrome, and are classified into typical and atypical carcinoids.
- MEN-1 syndrome is associated with up to 25% of cases of thymic carcinoids.
- Small biopsies and cytology cannot distinguish between atypical and typical carcinoid; surgical specimens are often required for classification.
- Surgery is the primary treatment modality for patients with localized disease and is the only curative option; while in Stage IV disease, there are few recommendations as to the approach to care.

INTRODUCTION

Carcinoid tumors arising in the lung and thymus are rare foregut neuroendocrine tumors (NETs) characterized by neuroendocrine morphology and differentiation and are classified using the World Health Organization (WHO) criteria, first described in 2004 and recently updated in 2015 (**Table 1**).[1] At one end of the spectrum are typical carcinoids (TC), which are low-grade, well-differentiated tumors that often present in early stage, rarely metastasize after surgical resection, and are generally relatively resistant to chemotherapy. At the other end of the spectrum are high-grade, poorly differentiated tumors such as small cell or large cell neuroendocrine carcinomas,

Disclosure Statement: The authors have nothing to disclose.
[a] Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, 300 East 66th Street, New York, NY 10065, USA; [b] Thoracic Oncology Service, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, 300 East 66th Street, New York, NY 10065, USA
* Corresponding author.
E-mail address: pietanzm@mskcc.org

Hematol Oncol Clin N Am 30 (2016) 83–102
http://dx.doi.org/10.1016/j.hoc.2015.09.003 **hemonc.theclinics.com**
0889-8588/16/$ – see front matter

Table 1
WHO 2015 classification for bronchial and thymic NETs

Nomenclature	Grade	Histopathologic Characteristics	Differentiation
Typical carcinoid	Low	Carcinoid morphology, <2 mitosis/2 mm^2, no necrosis, >0.5 cm diameter	Well differentiated
Atypical carcinoid	Intermediate	Carcinoid morphology, 2–10 mitosis/ 2 mm^2, or foci of necrosis	Well differentiated
Large cell carcinoma	High	NE structure, >10 mitosis/2 mm^2, necrosis (may be extensive), cytology resembling NSCLC, IHC positive for NE markers and/or NE granules by electron microscopy	Poorly differentiated
Small cell carcinoma		Small cell size, scant cytoplasm, nuclei with finely granular chromatin and absent or faint nucleoli, >11 mitoses/ 2 mm^2, extensive necrosis	

Abbreviations: IHC, immunohistochemistry; NE, neuroendocrine; NET, neuroendocrine tumors; NSCLC, non–small cell lung cancer; WHO, World Health Organization.

Adapted from Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization classification of lung tumors. Impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol 2015;10:1243–60.

which behave aggressively, often present with distant metastasis, and are sensitive to chemotherapy. Atypical carcinoids (AC) are considered to be well differentiated NETs, although they are intermediate grade and represent a more aggressive phenotype when compared with TC. In this review, the epidemiology and risk factors, as well as diagnostic and treatment paradigms, for typical and AC tumors of the lung and thymus are discussed. Owing to the rarity of these malignancies, treatment approaches have not been validated in large studies.

INCIDENCE, ETIOLOGY, AND PREDISPOSING GENETIC FACTORS

Bronchial Carcinoids

Bronchial carcinoids account for approximately 2% of all primary lung tumors and roughly 25% of all well differentiated NETs with an incidence rate ranging from 0.2 to 2 per 100,000 per year.[2–8] Over the past 30 years, the age-adjusted incidence rate of bronchial carcinoids has increased significantly, by approximately 6% per year.[3,4,8] This trend may represent the improvement in classification of these tumors, as well as the increase in use of imaging techniques that are able to detect asymptomatic disease. In the United States, there are nearly 6000 new cases per year.[9]

Most carcinoids of the lung are TC, with only 10% to 30% of bronchial carcinoids classified as AC.[6,10,11] Patients diagnosed with TC are approximately 10 years younger than those with AC, which occur in the sixth decade of life.[12,13] In children and adolescents, bronchial carcinoids are the most common primary lung neoplasm. These malignancies are found more commonly in women as compared with men and whites as compared with blacks.[8,12]

Currently, there are no clearly defined risk factors for bronchial carcinoids. Based on case series, patients with AC are more likely to be smokers as compared with patients with TC.[6,12,14] No other carcinogen or environmental exposure is implicated in the development of these malignancies.

Most bronchial carcinoids are sporadic tumors, although rare familial cases have been reported. In less than 5% to 10% of cases, bronchial carcinoids are associated