Functional Imaging Evaluation in the Detection, Diagnosis, and Histologic Differentiation of Pulmonary Neuroendocrine Tumors

Filippo Lococo, MD[a,*], Giorgio Treglia, MD[b], Alfredo Cesario, MD[c], Massimiliano Paci, MD[a], Angelina Filice, MD[d], Annibale Versari, MD[d], Pierluigi Filosso, MD[e]

KEYWORDS

• Pulmonary neuroendocrine tumors • pNETs • PET-CT scans • Radiometabolic evaluation

KEY POINTS

- Distinct features of different pulmonary neuroendocrine tumors (pNETs) include their pathologic characteristics as well as their clinical behavior, epidemiology, treatment, and prognosis.
- Typical carcinoids (TCs) are indolent neoplasms with a good prognosis, whereas atypical carcinoids (ACs) have a less indolent behavior with a certain propensity for metastatic spread. Both are well-differentiated pulmonary NETs are optimally treated with complete surgical excision.
- More aggressive pNETs, such as large cell neuroendocrine lung cancer and small cell lung cancer, often present with local invasion, thoracic lymph nodal metastases, and distant spread. As a result, affected patients may not be candidates for surgical resection and are treated with chemotherapy with or without radiation therapy, showing a poor prognosis.
- Taking into account the different biologic behavior of various pNET subtypes, achieving an accurate preoperative diagnosis is a key element for planning the best strategy of care.
- Recent evidence suggests that, even when surgery is indicated, the extent of both pulmonary resection and lymph nodal dissection are determined by the cytohistologic characteristics of pNETs.
- TCs and ACs share structural radiological findings and a clear differentiation is not possible through radiological findings only. The functional imaging evaluation using nuclear medicine techniques has improved in the last two decades with the aim of helping the physicians in the challenging clinical decision-making process of these rare entities.

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[a] Unit of Thoracic Surgery, Department of Nuclear Medicine, IRCCS-Arcispedale Santa Maria Nuova, viale risorgimento 80, Reggio Emilia 42121, Italy; [b] Department of Nuclear Medicine, Oncology Institute of Southern Switzerland, Bellinzona 6500, Switzerland; [c] Scientific Direction, IRCCS-San Raffaele Pisana, Via della Pisana, 235, Rome 00163, Italy; [d] Department of Nuclear Medicine, IRCCS-Arcispedale Santa Maria Nuova, viale risorgimento 80, Reggio Emilia 42121, Italy; [e] Department of Thoracic Surgery, University of Torino, via Giuseppe Verdi 8, Torino 10124, Italy

* Corresponding author.

E-mail address: filippo_lococo@yahoo.it

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- Because a certain or definitive diagnosis may not be easily obtained, radiometabolic evaluation represents a sort of noninvasive biopsy trying to correlate as accurately as possible the uptake pattern of pNETs (using different tracers) with the histologic types. Positron emission tomography (PET), using different tracers, has potential in the work-up process of pNETs. It may detect functional abnormalities even before the tumors become morphologically evident on conventional imaging.
- Not relying on dimensional criteria, PET is more accurate than conventional imaging for the disease extent assessment, restaging, and therapy response. Tracer uptake at PET imaging may be evaluated visually or by using semiquantitative measures such as the maximal standardized uptake value.
- The development of integrated PET-CT scans, has greatly contributed to a more accurate delineation of areas of increased tracer uptake, overcoming the limits of patients repositioning when the two images were acquired independently and fused afterward. Several PET tracers have been proposed for the evaluation of pNETs. The potential role of functional imaging evaluation using fluorine-18 fluorodeoxyglucose and somatostatin analogues labeled with gallium-68 in well-differentiated pNETs (TCs and ACs) with particular attention on clinical and surgical implications should be considered.

INTRODUCTION

It is well known that the distinct features among the different pulmonary neuroendocrine tumors (pNETs) include their pathologic characteristics as well as their clinical behavior, epidemiology, treatment, and prognosis. In addition, typical carcinoids (TCs) are indolent neoplasms with a good prognosis, whereas atypical carcinoids (ACs) have a less indolent behavior with a certain propensity for metastatic spread. Both these well-differentiated pNETs are optimally treated with complete surgical excision. Conversely, more aggressive pNETs, such as large cell neuroendocrine lung cancer (LCNEC) and small cell lung cancer (SCLC), often present with local invasion, thoracic lymph nodal metastases, and distant spread. Affected patients may not be candidates for surgical resection and are treated with chemotherapy with or without radiation therapy, showing a poor prognosis.[1,2]

Taking into account the different biologic behavior of various pNETs subtypes, the achievement of an accurate preoperative diagnosis is a key element for planning the best strategy of care in such patients.

Recent evidence suggests that even when surgery is indicated, the extent of both pulmonary resection and lymph nodal dissection are determined by the cytohistologic characteristics of pNETs.[2,3]

Unfortunately, TCs and ACs share structural radiological findings and a clear differentiation between these pNETs is not possible through radiological findings only.[4,5]

The functional imaging evaluation using nuclear medicine techniques has improved in the last two decades,[6] aiding physicians in the challenging clinical decision-making process for such rare entities. Because a certain or definitive diagnosis may not be easily obtained, the radiometabolic evaluation would represent a sort of noninvasive biopsy, which tries to correlate the uptake pattern of NETs (using different tracers) with the histologic types as accurately as possible.

Positron emission tomography (PET), using different tracers, has potential in the work-up process of pNETs. It may detect functional abnormalities even before the tumors become morphologically evident on conventional imaging. Moreover, not relying on dimensional criteria, PET is more accurate than conventional imaging for the disease extent assessment, restaging, and therapy response. Tracer uptake by PET imaging may be evaluated visually or by using semiquantitative measures such as the maximal standardized uptake value (SUVmax). Finally, the development of integrated PET-CT scans has greatly contributed to a more accurate delineation of areas of increased tracer uptake, overcoming the limits of patient repositioning when the two images were acquired independently and fused afterward.

Several PET tracers have been proposed for the evaluation of pNETs. This article, however, focuses on the potential role of functional imaging evaluation using fluorine-18 fluorodeoxyglucose (^{18}F FDG) and somatostatin analogues labeled with gallium-68 (^{68}Ga) DOTA-peptides in well-differentiated pNETs (TCs and ACs) with