A Population Based Pathology Analysis on Application of World Health Organization Nomenclature in Pulmonary Neuroendocrine Tumors

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Background
The WHO 2015 classification for pulmonary carcinoids, large cell neuroendocrine carcinoma (LCNEC) and small-cell lung cancer (SCLC) is in essence unchanged compared to the previous one (1999 and 2004)1. This despite known limitations in the diagnostic process, such as:
- Infrequent exposure in daily pathology practice (carcinoids/LCNEC)
- Impossibility to classify carcinoids/LCNEC on limited material (biopsies)
- Different nomenclature systems (gastrointestinal vs. pulmonary)2

Study aims
1) To analyze if the nomenclature used in daily practice to describe the diagnoses of pulmonary carcinoids, LCNEC and (non-small cell) carcinomas with immunohistochemical differentiation, is in line with the recommended WHO 1999/2004 classification terminology.
2) To examine differences between physicians and pathologists in interpretation of retrieved non-WHO nomenclature diagnoses.

Methods:
Retrospective analysis of conclusions of pathology reports selected from PALGA (the Dutch Pathology Registry) from 01-2003 to 12-2012

Inclusion criteria for PALGA search:
- Anatomic location: lung/bronchus/pleura/mediastinum
- Primary tumor/metastasis: NET grade 1-3, LCNEC, (atypical/typical) carcinoid and all carcinomas with text keyword “endocrine”.

Exclusion criteria used while screening conclusions:
- Non-pulmonary or undefined origin
- Without final conclusion (i.e. differential diagnosis)
- SCLC diagnosis
- Cases were selected for final revision (if applicable) or largest tissue specimen

Retrieved diagnoses were scored and clustered for the following variables:
- Diagnostic cluster: carcinoid, high-grade neuroendocrine carcinoma, carcinoma with neuroendocrine features/differentiation and neuroendocrine tumor n.o.s.
- Non-WHO nomenclature (i.e. the terminology in accordance with the recommended WHO 2004 classification yes/no?). For recommended nomenclature all diagnoses were strictly compared with the WHO 2004 manual3

Online questionnaire non-WHO nomenclature:
- Non-WHO nomenclature diagnoses retrieved through the screening were presented to N=35 physicians and N=19 pathologists.
- Participants were requested to cluster the non-WHO nomenclature diagnoses into one of the WHO 2004 classification categories or as unknown4

Results
7989 conclusions were screened, after applying the exclusion criteria conclusions from 3216 unique patients were selected for analyses. This included N=3052 patients with a conclusive diagnosis.

15% of retrieved diagnoses had applied non-WHO nomenclature

Conclusions
- In 15% of pulmonary neuroendocrine tumors other than SCLC, a non-WHO nomenclature diagnoses was given, this occurred more frequently on smaller tissue specimens
- Usage of non-WHO nomenclature may lead to misunderstanding among physicians and pathologists
- Whether nomenclature deviates from the WHO is due to pathologist’s preferences or to difficulties fitting the current classification (on small tissue samples), remains to be examined.

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