Lung adenocarcinoma: a new histological classification

Algorithm for the subtyping of NSCLC

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Introduction

More and more Patient and Tumour-tailored treatments -
- Need for biological markers
  • EGF
  • KRAS
  • ERCC1 and RRM1
- Need for accurate diagnosis for specific treatments
  • SCLC vs NSCLC
  • NSCLC: SCC vs ADC

Introduction

Lung cancer
- Frequent

- Adenocarcinoma is the most frequent subtype, representing 35 to 40% of all lung cancers
- Differential diagnosis may be difficult especially on cytological material and on small biopsy fragments, representing 85% of the received diagnostic material

Adenocarcinoma

1.3.3. Adenocarcinoma
- Acinar
- Papillary
- Bronchioloalveolar carcinoma
- Non-mucinous
- Mucinous
- Mixed mucinous and non-mucinous or adenocarcinoma of special type
- Solid adenocarcinoma
- Adenocarcinoma with mixed patterns
- Variants
- Well-differentiated fetal adenocarcinoma
- Malignt adenomatous hyperplasia
- Clear cell adenocarcinoma

Lung adenocarcinoma

Definition:
- Malignant epithelial tumour characterized by glandular differentiation or signs of mucin production
- Heterogeneous group of histologically very different tumours
- The mixed variant is the most frequent subtype, representing 80 to 90% of all adenocarcinomas
Adenocarcinoma

Proposal of a new classification for adenocarcinomas

- Preinvasive lesions
  - Atypical adenomatous hyperplasia
  - In situ adenocarcinoma (BAC pattern)
    - Non-mucinous
    - Mucinous
  - Adenocarcinoma with minimal invasion (lepidic growth pattern with an invasive foci ≤ 5mm or <10% of invasion)
- Invasive adenocarcinoma
  - Classical forms (lepidic pattern, acinar, papillary, micropapillary and solid)
  - Variants (mucinous or colloid, cystadenocarcinoma and fetal adenocarcinoma)

FIGURE 7. Survival curves according to the WHO classification. The 5-year disease-free survival rates are 100% (BAC), 72.4% (mixed subtypes), 53.6% (solid), and 42.9% (papillary), respectively.

Solid: minimum 2 hpfs with at least 5 mucin containing cells
Preinvasive lesions

- Atypical adenomatous hyperplasia (AAH)
  - Precursor of ADC
  - <5 mm
  - In the vicinity of ADC

BAC

- Defined as growth of tumour cells along preexisting alveolar walls (lepidic growth pattern) without invasion of stroma, vessels or pleura and absence of metastases
  - => by definition: diagnosis is not possible on small biopsies or cytology

BAC

- Pure form:
  - < 2 cm
  - Rare: 3-4% of NSCLC
  - Pure ground glass aspect on CT
  - In situ adenocarcinoma with a 100% 5 year survival
- Minimally invasive:
  - < 2 cm
  - Invasive foci less than 5 mm
- BAC multifocal and bilateral:
  - Mostly mucinous forms
  - Often invasive component
- Mixed adenocarcinoma with a BAC component

Pure BAC

BAC minimally invasive
Sakurai’s classification

BAC mucinous, multifocal

Mixed Adenocarcinoma, acinar and BAC

Quiz
What is your diagnosis?

Peripheral lung adenocarcinoma
1. Adenocarcinoma NOS
2. Adenocarcinoma mixed subtype
3. Bronchioloalveolar carcinoma, Sakurai grade 3
4. Adenocarcinoma with minimal invasion

How should a BAC be measured?
1
2

What is your diagnosis?

Bronchioloalveolar carcinoma
1. Yes
2. No

For an accurate diagnosis

- Histology first:
  - 4 main subtypes:
    - SCC
    - ADK
    - LCLC
    - SCLC

- If needed, IHC for DD SCLC vs NSCLC
What type of specimen?
- Surgical resections
- Paraffin-embedded biopsies
- Cytology
  - Fresh (unfixed)
  - Alcohol-fixed (monolayer)
  - Paraffin-embedded cell blocks
- Frozen material

Belgian algorithm proposed by the Belgian Mesothelioma Registry

SCLC
- Chromogranin
- Synaptophysin

NSCLC
- Histology
- SCC
- Indetermined
- ADC
Solid form of adenocarcinoma: at least 5 mucin containing cells in minimum 2 HPF.

Concordant

- CK7 +
- TTF1 ±
+ p63 -
± CK5,6/34βE12 -

SCC ADC

Concordant

- CK7
- TTF1 ±
+ p63 -
± CK5,6/34βE12

SCC ADC
With the exception of a strong and diffuse staining for p63 and CK5/6E12, which is in favor of an SCC.

Conclusion

- Proposal of a new classification for lung adenocarcinomas based on survival curves
- A diagnosis of BAC cannot be done on cytology or small biopsies
- Numerous subtypes of adenocarcinoma, the mixed subtype being the most frequent one
- Proposal of a Belgian algorithm for the subtyping of NSCLC