Lung Cancer Associated with Cystic Airspaces: Don’t Let This Lesion Fool You!

Annemie Snoeckx

Antwerp University Hospital, University of Antwerp, Belgium
Head of Department: Prof. dr. Paul M. Parizel

Co-authors: Pieter Reyntiens, Maarten J. Spinhoven, Laurens Carp, Paul E. Van Schil, Patrick Pauwels, Jan P. van Meerbeeck, Paul M. Parizel

Thoracic Oncology Group @ UZA
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Overview

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1. Learning objectives

- To illustrate the spectrum of imaging findings of “lung cancer associated with cystic airspaces”
- To define key imaging features
- To discuss and illustrate differential diagnoses
2. Background

- Lung cancer is the leading cause of cancer deaths worldwide.
- It typically presents as a mass or nodule, round or oval in shape. Recognition of these typical cases is often straightforward, whereas diagnosis of uncommon manifestations is more challenging.
- “Lung cancer associated with cystic airspaces” is an uncommon entity becoming more frequently recognized.
- It comprises cancer arising or abutting the wall of a “pulmonary cystic airspace.”
- These cyst-like lesions have been called cysts, bullae, blebs, ... Mostly the generic term ‘cystic airspaces’ is used: it indicates discrete thin-walled air-containing spaces in the lung regardless of the pathologic findings.
2. Background

- Patients are mostly smokers
- **Incidence**
  - Represented 3.6% of screen-detected tumors in I-ELCAP lung cancer screening trial
  - Kaneda et al. reported an incidence in the same range: 3.5% in a group of 545 surgical cases
- These cancers are generally **aggressive**
- Possible **mechanism**: check-valve obstruction at the terminal bronchiolar level by an inflammatory or neoplastic process that leads to formation of the cystic airspace
2. Background

- **Histopathology**
  - The cystic airspace can have different histologic features
  - Lung cancer component of the lesion can be any histology, but mainly is adenocarcinoma and squamous carcinoma to a lesser extent

- **Lung Cancer Screening**
  - 22.7% (5/22) of missed carcinomas in the NELSON lung cancer screening trial presented as bulla with wall thickening
  - Lung cancer screening (trials) will give more insight into the progression of these cancers and might help in answering questions
3. Imaging findings

- Mascalchi et al. described 4 types of morphologic patterns on CT
  - **Type 1**: presence of a nodule extruding from the wall of the cystic airspace
  - **Type II**: nodule confined within the lumen of the cystic airspace
  - **Type III**: soft tissue density extending along the wall of the cystic airspace
  - **Type IV**: solid or nonsolid tissue intermixed within cluster of multiple cystic airspaces
3. Imaging findings

- Evolution: uniformly thin wall of the airspace, becoming thicker with increased circumferential involvement and nodule formation between 12 and 118 months after initial CT scan.
- No histologic features identified that suggested preexisting congenital cystic lung disease nor presence of a preexisting cavity.
- Associated emphysema is often present.
- When the solid part of the lesion increases, the diameter of the cystic airspace can decrease, increase or remain stable.
3. Imaging findings

- 18F-FDG-uptake is variable, ranging from absent or mild to moderate or marked

- This is related to two facts
  - When the predominant tumor component presents as lepidic growth, FDG-uptake can be mild or absent. These lesions often present on CT as ground-glass
  - The cystic component of the lesion itself does not show 18F-FDG-uptake
4. Cases

CASE 1
72-y-old man with a previous history of head and neck cancer who presented during follow-up with an irregular thickening of the wall of a cystic airspace in the right lower lobe. Within an extremely short time period of 3 months, the lesion had grown, filling the cystic airspace and presenting as a solid nodule. Diagnosis of primary lung cancer (squamous cell carcinoma) was confirmed after transthoracic biopsy.
CASE 2

57-y-old woman who presented with a cystic airspace in the left upper lobe. In the periphery of the lesion there were two irregular nodules: one at the top and one at the bottom of the cystic airspace. Both nodules showed a high uptake on 18F-FDG-PET. Lobectomy was performed and histopathology confirmed the diagnosis of a cystic airspace with two nodular foci of adenocarcinoma.
CASE 3
72-y-old woman in whom as incidental finding a subpleural cystic airspace was seen in the left lower lobe. The medial wall of the cystic airspace showed a bandlike thickening. Follow-up CT 6 months later showed an increase of the exophytic component with more nodular aspect as well as a change of the internal structure of the cystic airspace. Lobectomy was performed and histopathology showed an invasive adenocarcinoma.
CASE 4

76-y-old man who presented with a subpleural nodule with associated cystic airspace in the left lower lobe. The lesion showed a very high uptake of 18F-FDG PET. Transthoracic biopsy confirmed the diagnosis of squamous cell carcinoma. Follow-up after radiotherapy treatment of the malignant lesion in the left lower lobe showed a nodule abutting the wall of a cystic airspace in the right lower lobe. Growth of this nodule was demonstrated after a second follow-up examination another 3 months later; findings were suspicious for a second primary.
CASE 5

68-y-old woman who presented with numerous nodules in both lungs: large spiculated solid nodules (perihilar region right upper lobe), part-solid nodules, pure ground glass nodules as well as 3 lesions presenting as lung cancer associated with cystic airspace (blue arrows). Diagnosis of adenocarcinoma was histopathologically proven in the large spiculated solid lesion in the right upper lobe and in the cystic airspace lesion with solid component in the left lower lobe.
CASE 6

74-y-old man who presented with a large cystic airspace surrounded and interspersed with ground glass. The lesion remained stable during a 3 month period of follow-up making an infectious lesion unlikely and the morphology of the lesion was found to be suspicious for lung cancer. 18F-FDG-PET showed only very minor uptake. Lobectomy was performed. Histopathology confirmed the diagnosis of lung cancer and showed a NSCLC with predominant lepidic pattern. These findings are consistent on imaging with the ground glass aspect of the abnormalities and are an explanation for the very low 18F-FDG-uptake on PET.
CASE 7

78-y-old man who presented with a persistent triangular area of cystic changes surrounded by an area of consolidation. Over time the area changed in morphology with decrease of the cystic airspaces and increase of the consolidation. Lobectomy was performed and histopathology showed an invasive adenocarcinoma.
CASE 8
Area of consolidation with central foci of cystic airspaces in the right lower lobe in a 69-year-old man. During follow-up the lesion showed an increase in size and density. Diagnosis of adenocarcinoma was confirmed on histopathology.
5. Differential diagnosis

- Depends on the type (I-IV) of lung cancer associated with cystic airspace
- Differential diagnosis is broad and includes a variety of solitary cavitary lung lesions: tumor, infection, granulomatous disease, bronchogenic cyst, ...
- Entities that may mimic type IV are diffuse centrilobular emphysema with superimposed ground glass or consolidation, large pulmonary infarct, ...
- Look for associated findings to narrow down a differential diagnosis list
- Clinical information, evolution and previous medical history are crucial for assessing the right diagnosis
Old tuberculous cavern with small fungus ball (Candida)

Infected bronchogenic cyst

Cavitated lung infarct

Squamous cell carcinoma
Emphysema with superimposed infectious consolidation

Large pulmonary infarct

Adenosquamous carcinoma
6. To remember

- Lung cancer associated with cystic airspaces is a relative new entity, getting more attention
- Closely look at the wall of cystic airspaces, especially when they are new
- Nodules, consolidation or ground-glass surrounding or abutting cystic airspaces should be closely monitored
- Early recognition is important to avoid delay in diagnosis and treatment
- Lots of questions remain and further research is needed
  
  When to consider malignancy? What regimen of follow-up?
  Are all 4 types of the same concern? ...
'You only see what you look for and you only look for what you know'

Don’t forget to think about “lung cancer associated with cystic airspaces” when you read chest CT’s
7. Suggested readings


Author contact information

Annemie Snoeckx, MD

Antwerp University Hospital
Radiology Department
Wilrijkstraat 10
2650 Edegem, Belgium

annemie.snoeckx@uza.be

www.uza.be
www.uantwerpen.be