Bronchioloalveolar carcinoma: imaging findings and follow-up

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Advanced Radiology Clerkship, BIDMC
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Agenda:

• Patient case presentation
• Definition & epidemiology of bronchioloalveolar carcinoma (BAC)
• BAC as a solitary pulmonary nodule (SPN)
• Challenges in diagnosis
• Treatment and follow-up
Patient Presentation

- 78-year-old non-smoking woman presents with chest pain
- EKG and laboratory values are within normal limits
- Imaging work-up was completed
Our patient: Frontal and Lateral Chest X-ray

Chest X-ray
NORMAL

Image from BIDMC PACS
Our patient: Lesion on Axial Chest CT

12 mm non-calcified ground glass opacity (GGO) in right lower lobe
Our patient: CT-Guided Biopsy

Pathology results:

Minute fragments of pulmonary alveolar parenchyma

No evidence of malignancy

Image from BIDMC PACS
Our patient: Growth on Serial CT

Diagnosis: Bronchioloalveolar carcinoma (BAC)

Images from BIDMC PACS
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BAC - Definition

- Subset of lung adenocarcinoma (NSCLC)
- Develops from terminal bronchiolar and acinar epithelia
- Growing along alveolar septa, no vascular or pleural involvement (lepidic growth)
- Pure BAC is non-invasive, but with spread is called “adenocarcinoma of mixed subtype, with predominant BAC”

BAC - Epidemiology

- Increasing interest due to increasing prevalence and unique clinical, radiologic, and epidemiologic (incidental detection and screening)

- Pure BAC - 4% of lung cancers, mixed BAC and adenocarcinoma - > 20% of all NSCLCs

- Disproportionately affects women (up to 50%), never-smokers, and Asians

- Most common lung cancer in nonsmokers and former smokers
BAC - Clinical presentation

- 50% asymptomatic
- 50% variable symptoms
  - weight loss, bronchorrhea, dyspnea
  - chest pain, hemoptysis, fever, cough
Lecture Overview:

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BAC – Solitary pulmonary nodule

Density

- Ground Glass (GGO)
- Part-Solid (PS)
- Solid (S)

Courtesy of Dr. Diana Litmanovich
BAC: Rad /Path correlation with Noguchi Classification System

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Histopathologic Description</th>
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<tbody>
<tr>
<td>A</td>
<td>Localized pure BAC (GGO)</td>
</tr>
<tr>
<td>B</td>
<td>Localized BAC with foci of alveolar collapse (PS)</td>
</tr>
<tr>
<td>C</td>
<td>Localized BAC with active fibroblastic proliferation (PS)</td>
</tr>
<tr>
<td>D</td>
<td>Poorly differentiated adenocarcinoma (S)</td>
</tr>
</tbody>
</table>

![Diagram of BAC subtypes]

Courtesy of Dr. Diana Litmanovich
Noguchi type A adenocarcinoma – pure ground glass opacity (GGO)

H&E, High power

Noguchi type B adenocarcinoma – GGO with a solid component

H&E, Low power

Alveolar collapse (invasion)

Noguchi type C adenocarcinoma - Solid nodule with peripheral GGO

H&E, Low power

Noguchi type D adenocarcinoma - Solid nodule with spiculated margins

H&E, Low power

Clinical Relevance

• As BAC component increases, better prognosis

• Type A and B (Noguchi classification) have more GGO component – excellent outcome s/p resection and lower recurrence rates

• GGOs show less potential for metastases than solid lesions
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BAC as SPN: DDx of Persistent Focal GGO

- AAH – atypical adenomatous hyperplasia
- Focal interstitial fibrosis
- Focal Organizing pneumonia
- Lymphoproliferative disorder

75% of 53 GGOs  

**NO** morphologic features to distinguish BAC on thin section CT from other GGO nodules
BAC as Persistent Focal GGO: High index of suspicion

- Slow increase in size
- Development of solid component
- Stable size and increasing density

Hasegawa et al Br J Radiol 2000
Slowly growing BAC

2004

2005

2006

Courtesy of Dr. Diana Litmanovich
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BAC - Treatment options

- BAC presenting as a SPN - surgical resection
- Promising results with targeted chemotherapy agents:
  - gefitinib
  - erlotinib
  - cetuximab
- Interfer with the epidermal growth factor receptor
- **Favorable responders:** women, nonsmokers, and those with adenocarcinoma (particularly BAC)
How are small pulmonary nodules followed?

- **Former standard of practice → all non-calcified pulmonary nodules were considered potentially malignant**
- **<1% of small nodules** in patients without history of carcinoma were malignant
- **Downside**: surgery, limited resources, health care costs, patient anxiety
Creating new guidelines: Studies

• Early Lung Cancer Action Project
  – > 60 yrs-old, >10 year pack history
  – 23% non-calcified, 2.7% malignancy

• Mayo Clinic Lung Cancer Screening Trial
  – > 50 yrs-old, > 20 year pack history
  – 69% noncalcified nodules, 2.6% malignancy

• MGH Radiology (Benjamin et al)
  – 10 (11%) malignancies (9 metastases)
  – <1% in those without known neoplasm
Creating new guidelines: Variables

- **Nodule size**
  - Likelihood of malignancy increases with size
    (1% for < 5mm vs 18% for 8-20 mm)

- **Growth rate**
  - Doubling times vary for ground-glass vs. solid
  - Extended follow-up intervals for nonsolid/partly solid

- **Relative Risk**
  - 10x greater RR for male smokers vs. non-smokers
  - Malignant nodules grow faster in smokers
  - Lung cancer is uncommon in patients < 35 years
Management Approach: Fleischner Guidelines for Incidentally Detected Nodules in Persons > 35 yrs

Low Risk*

- < 4 mm: No FU needed
- > 4-6 mm: CT @ 12 months. If no Δ, no further FU
- > 6-8 mm: CT @ 6-12 months, if no Δ, then again at 18-24
- > 8 mm: CT @ 3, 9, and 24 mo; contrast CT, PET, or bx

*Minimal or absent smoking hx, and no other risk factors.
Management Approach: Fleischner Guidelines for Incidentally Detected Nodules in Persons > 35 yrs

High Risk

- **< 4 mm**
  - CT @ 12 months. If no Δ, no further FU

- **> 4-6 mm**
  - CT @ 6-12 months, if no Δ, then again at 18-24

- **> 6-8 mm**
  - CT @ 3-6, 9-12, and 18-24 months

- **> 8 mm**
  - CT @ 3, 9, and 24 mo; contrast CT, PET, or bx
Follow-up Take Home Points

• Nodule size, growth rate, and relative risk of patients

• These guidelines are for incidentally discovered nodules that are not changing.

• If nodules grows between two studies, individual work-up is needed.
Caution in Guideline Usage

• Young patients: Primary lung cancer is rare in patients < 35-years-old. **No need** for multiple CT studies → instead single low-dose in 6-12 months

• Known malignancy: Potential lung metastases should be followed with **more frequent** CT scans

• Unexplained fever: Nodule may represent **active infection**, therefore short term imaging or intervention may be necessary
Summary

- Patient → 78-yr-old non-smoker, female
- BAC is a subset of adenocarcinoma, appearing as a GGO
- BAC histology correlates with favorable prognosis: longer survival, less metastasis, less recurrence
- Fleischner guidelines for incidentally detected nodules on CT
Acknowledgments

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References

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