Use of Integrated PET CT in the Clinical Staging of Non Small Cell Lung Cancer

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Clinical Presentation

- 79yo woman with cough productive of green sputum worse than baseline cough, exertional SOB and 12 lb unintentional weight loss in 1 mo
- Denies fevers, night sweats or CP
- PMH: COPD, HTN, CAD, DM2
- SoH: 54 pack-yr hx of smoking cigarettes, quit 5 yrs ago
- PE: afebrile, 02 sat 95% RA, good air movement, mild end-exp wheezing, fine crackles in left lung that resolved after cough
Interval History

- PCP prescribed Azithromycin x5 days for presumed CAP
- Cough and SOB did not improve
- Re-presented to care and received CXR
Our Patient: Suspicious LUL mass

Frontal Scout CXR

BIDMC, PACS

3cm

Lateral Scout CXR

BIDMC, PACS

There is a **3cm rounded, non-calcified opacity** without distinct borders or air-fluid level in the left upper lung at the level of aortic knob. There is **right tracheal deviation** at the level of the opacity suggesting a mass effect. There is no obvious LAD in the hilar or mediastinal lymph node regions, although the A/P window is difficult to assess given the proximity of the mass.
Ddx of Solitary Pulmonary Mass
(<4cm in diameter)

• Common
  - Carcinoma of the lung
  - Metastasis

• Uncommon
  - Abscess, AV malformation, Carcinoid,
    Granuloma, Hematoma, Lymphoma, Round
    Atelectasis, Fungus ball, Fluid-filled cyst

The mass abuts the major fissure with posterior bulging of the major fissure. The anterolateral border of the mass is spiculated.

The mass also abuts the left upper lobe bronchus without evidence of invasion. However, there is narrowing of the upper lobe bronchus.
Our Patient: Distinct features of LUL mass

Axial C+ CT Chest

Using soft tissue windows, we see that the tumor is continuous with the mediastinum but there is no evidence of mediastinal invasion. There is a clear ring of high attenuation in the periphery of the mass, suggesting central necrosis. There is a hyperlucent area at the posterior side that could represent an air filled cavity or post obstructive bronchiectasis. The vessel en face likely represents the tumor’s blood supply.
T in TNM Staging

- Based on these images, we know that our patient’s tumor has a diameter of 3 cm so it is considered stage T1b.

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T1</strong></td>
<td>Tumor ≤3 cm diameter, surrounded by lung or visceral pleura, without invasion more proximal than lobar bronchus</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor ≤2 cm in diameter</td>
</tr>
<tr>
<td><strong>T1b</strong></td>
<td>Tumor &gt;2 cm but ≤3 cm in diameter</td>
</tr>
<tr>
<td><strong>T2</strong></td>
<td>Tumor &gt;3 cm but ≤7 cm, or tumor with any of the following features:</td>
</tr>
<tr>
<td></td>
<td>Involved main bronchus, ≥2 cm distal to carina</td>
</tr>
<tr>
<td></td>
<td>Invades visceral pleura</td>
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<tr>
<td></td>
<td>Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor &gt;3 cm but ≤5 cm</td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor &gt;5 cm but ≤7 cm</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>Tumor &gt;7 cm or any of the following:</td>
</tr>
<tr>
<td></td>
<td>Directly invades any of the following: chest wall, diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, main bronchus &lt;2 cm from carina (without involvement of carina)</td>
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<tr>
<td></td>
<td>Atelectasis or obstructive pneumonitis of the entire lung</td>
</tr>
<tr>
<td></td>
<td>Separate tumor nodules in the same lobe</td>
</tr>
<tr>
<td><strong>T4</strong></td>
<td>Tumor of any size that invades the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, or with separate tumor nodules in a different ipsilateral lobe</td>
</tr>
</tbody>
</table>
Let’s determine this patient’s nodal stage.
Our Patient: Bilateral hilar lymphadenopathy

There are areas of soft tissue attenuation that are >1cm in diameter and located in the right and left hilar regions, likely representing bilateral hilar lymphadenopathy. While thoracic lymph nodes can vary in size, a short axis diameter >1cm is considered abnormal.
N in TNM Staging

• Our patient has contralateral hilar LAD which equates to stage N3.

<table>
<thead>
<tr>
<th>Regional lymph nodes (N)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastases</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).</td>
</tr>
</tbody>
</table>
Our patient: “Tree in bud”

There are tubular and nodular opacities in the lung periphery consistent with a “Tree in bud” sign. A classic Tree in Bud is shown at right.

What is “Tree in bud” sign?

• Descriptive term reserved for CT
• Represents peripheral bronchioles with mucus plugging, bronchial dilatation, wall thickening
• Most commonly refers to infectious process but can be present in inflammatory or congenital disorders, neoplasms, aspiration of irritants, idiopathic pulmonary diseases
• In this pt, could represent endobronchial invasion of tumor with tumor nodules or post-obstructive inflammatory or infectious process
Our Patient: Incidental finding of multiple renal masses

C+ CT Chest

There are several small irregular heterogeneous areas of soft tissue attenuation seen on both of the images with thinning of the cortex and deformation of the normal kidney architecture. MRI abdomen is needed to characterize these lesions.
Our Patient: Multiple enhancing renal masses

There is a rounded low signal area within the right kidney (left image) that enhances with contrast (right image), indicating that this is a vascularized area and not just a simple cyst.
Why is a tissue diagnosis needed?

- Since renal and lung cancers are treated differently, must obtain tissue diagnosis
- The following procedures were performed:
  - Endobronchial U/S-guided transbronchial lung biopsy
  - CT-guided renal biopsy
Our Patient: Pathology specimen

40X: H&E stained section from core needle biopsy of kidney

Normal Tumor

200X: H&E stained section of lung from transbronchial biopsy

Alveolar tissue is seen with occasional neutrophils. No tumor is present.

200X: H&E stained section from core needle biopsy of kidney

Nest of malignant tumor cells with a high N:C ratio, abundant mitoses and focal necrosis. Consistent with metastatic squamous cell carcinoma.

Since SCC does not arise in the kidney, it is most likely primary lung cancer with renal metastasis.

Slide courtesy of Hannah Gilmore MD, Pathology Dept, BIDMC
Radiologic Features of SCC of Lung

- Ranges in size from 1-10cm
- Centrally located, although 1/3 of SCC are found beyond the segmental bronchus
- Because of the central location, can cause post-obstructive pneumonia or atelectasis which occurs in up to 50% of cases
- Cavitate in 10-20% of cases, particularly in large peripheral lesions
- Most common sites for metastases from SCC of the lung are adrenal, kidney, bone and liver

We believe this patient has renal metastases. Let’s confirm this and determine if there are other sites of metastases.
M in TNM Staging

• In the past, has been done by PET alone or CT alone
  – Advantage of PET: detect smaller lesions that can’t be resolved by CT; limit detection to fast-growing tumors, which are more likely to be malignant
  – Advantage of CT: understand exact location of lesion

• Now combined PET CT is being used

• Images can either be displayed side by side and correlated visually by the radiologist or directly overlaid: 2003 NEJM trial showed that direct integration of images has better diagnostic accuracy than visual correlation
Integrated PET CT

- **Physiologic positives**: brain, heart, GI tract, genitourinary tract, recently exercised muscle
  - Cannot be used reliably for brain metastases, so many undergo separate MRI brain
- **False positives**: Benign tumors such as sclerosing hemangioma, leiomyoma, inflammatory pseudotumor, any areas of inflammation, atherosclerosis (aorta), granulation tissue, in pleura after pleurodesis, after placement of central lines, chest tubes, gastrostomy tubes, after mediastinoscopy
- **False negatives**: slow growing tumors such as BAC, carcinoid, mucoepidermoid carcinoma
# Sensitivity and Specificity of PET CT in NSCLC Staging

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td><strong>Tumor</strong></td>
<td>38-90%</td>
<td>40-90%</td>
</tr>
<tr>
<td>(Chest wall invasion)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nodes</strong></td>
<td>79-85%</td>
<td>89-92%</td>
</tr>
<tr>
<td>(Mediastinal lymph nodes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mets</strong></td>
<td>88-100%</td>
<td>100%</td>
</tr>
<tr>
<td>(to liver and adrenal glands)</td>
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</tbody>
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Radiation Exposure in PET CT

- More than either study alone
  - (~18mSv from CT, ~7mSv from FDG)
- Effective dose depends on:
  1) **scan parameters** such as **tube current** and potential, pitch factor and slice collimation
  2) **scanner factors** such as beam filtration and beam-shaping filter
  3) **length of the scan region**

- 50% reduction in **tube current** reduces radiation dose by half, but unfortunately increases image noise
- Therefore, current protocols use 80mA current to optimize image quality but decrease radiation exp
Our Patient: Increased tracer uptake in kidney and bone

Renal mass also showed high tracer uptake but is not shown here.
M in TNM Staging

- Our patient has confirmed metastases to kidney and newly discovered metastases to bone, which equates to stage M1b.

<table>
<thead>
<tr>
<th>Distant metastasis (M)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural or pericardial effusion</td>
</tr>
<tr>
<td>M1b</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
Overall Clinical Staging for NSCLC

- We can correlate this patient’s TNM stage to overall clinical stage. T1bN3M1b correlates to Clinical Stage IV, which is considered unresectable.

<table>
<thead>
<tr>
<th>Stage groupings</th>
<th>T1a-T1b</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1a,T1b,T2a</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T1a,T1b,T2a,T2b</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any N</td>
<td>M1a or M1b</td>
<td></td>
</tr>
</tbody>
</table>

Treatment

• For elderly patients with advanced NSCLC, treatment depends on the individual’s goals of care

• However, platinum-based systemic chemotherapy is the chemotherapy regimen of choice when appropriate

• Our patient began cisplatin/gemcitabine regimen
Prognosis in NSCLC depends on clinical stage

- Median survival for our patient is 6mo.
Summary

• Common presenting symptoms of a pt with lung cancer
• Differential of a single rounded opacity on CXR
• Normal anatomy of thoracic lymph nodes
• Use of IR-guided procedures to obtain a tissue diagnosis of a suspected malignancy
• Sensitivity and specificity of integrated PET CT and use of PET CT in clinical staging of NSCLC
• Treatment of and prognosis for patients with NSCLC
References


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