Radiation-Induced Lung Injury

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Our Patient

D.C. is a 50 year-old woman with a 30-pack year history of smoking who presented to the ED because she felt like her “rib was popping out”.

A chest film was obtained.
Our Patient: Presenting CXR

Finding: Focal opacity in the right middle lung zone

- No rib fractures and no pneumothorax were seen
# Diff Dx of Solitary Pulmonary Nodule

<table>
<thead>
<tr>
<th>Neoplasm:</th>
<th>Vascular:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Primary/Bronchogenic (AdenoCA, Squamous Cell CA, large cell CA, Small Cell CA, bronchioloalveslar)</td>
<td>AVM Infarct</td>
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<tr>
<td>B. Harmartoma</td>
<td><strong>Trauma:</strong> Pulmonary Contusion</td>
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<tr>
<td>C. Solitary Metastasis</td>
<td><strong>Other:</strong> Congenital Connective tissue disease</td>
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**Infection:**
- Pneumonia
- Abscess
- TB
- Fungal (Aspergillus)
Our Patient:

Our patient had no previous films available for comparison.

She had no signs of infection, making an infectious etiology less likely.

Because she was a smoker over age 30, a CT was obtained.
**Finding:** Right hilar 2.5 cm mass which obstructs the right middle lobe bronchus with resultant atelectasis.

Finding: Loss of fat plane adjacent to the right heart border.

Because this may indicate pericardial invasion, an MR was obtained to better characterize the nodule.
Our Patient: MR of Nodule

**Finding:**
Area where pericardial fat adjacent to the mass is obliterated, highly suggestive of pericardial invasion
Our Patient: Course

Diagnosis:
- Bronchoscopy and mediastinoscopy → No nodal malignancy
- Bone scan → Negative for metastases
- Head CT → Negative for metastases
- CT – guided biopsy of right hilar mass → Non-small cell lung CA

Dx: Stage T4, N0, M0 or Stage IIIB lung carcinoma

Treatment:
- Our patient started on a chemoradiation therapy protocol
  - Cycle #1: Taxol and Carboplatinum therapy x 1 month
  - Cycle #2: Taxol and Carboplatinum PLUS daily XRT x 1 month

★ One month after receiving the second cycle of therapy, our patient presented with dyspnea, cough with clear sputum, and fevers to 101. A chest x-ray and chest CT were obtained.
Diagnostic Dilemma: Plain Films

**Finding:** Prominent interstitial infiltrate. Primarily involving right lower lung field.

**Finding:** Infiltrate also affects perihilar regions bilaterally and apices of both lungs.

**Note:** Right hemidiaphragm is elevated.
Diagnostic Dilemma: CT

**Finding**: Geographic paramediastinal linear opacification

**Finding**: Diffuse ground glass opacification in right lung and left apex

Because the linear opacification does not respect normal anatomic boundaries, radiation-induced lung injury was suspected. But, are the other findings consistent with this diagnosis?
What is Radiation-Induced Lung Injury?

**Epidemiology:**

Incidence varies depending on regimen and field used. Factors influencing development of injury include volume of lung irradiated, dose of radiation, frequency of dose, and use of concurrent chemotherapy.

One study reported clinical pneumonitis in 5-15% of lung cancer patients; 0-10% of breast cancer patients; and 0% of mediastinal lymphoma patients. (Ref 8)

Radiologic abnormalities are typically seen at much higher rates than clinically apparent pneumonitis.
What is Radiation-Induced Lung Injury?

**Pathogenesis:** 2 Stages of Damage

1) **Early** (1-6 months post-radiation): “Cellular Infiltration”
   Diffuse alveolar damage (particularly type II cells). Cells and plasma enter into alveolar spaces.
2) **Late or Chronic** (6 or more months post-radiation): “Fibrosis”
   Progressive alveolar thickening and vascular sclerosis

**Clinical Presentation:** 2 Syndromes

1) **Radiation Pneumonitis:** Onset 1-3 months following radiation therapy.
   Symptoms include dyspnea, cough, fever
2) **Radiation Fibrosis:** Evolves 6 months to 2 years following radiation therapy.
   Symptoms are primarily dyspnea; may develop cor pulmonale and sx of CHF
Diff Dx of Radiation-Induced Lung Injury

- Recurrent Neoplasm
- Lymphangitic Spread of Neoplasm
- Infection
  - Bacterial
  - Viral
  - Fungal
- Chemical Pneumonitis
  - Inhalation exposures
  - Chemotherapy-induced
Menu of Tests for Evaluation of Radiation-Induced Lung Injury

- **Chest Plain Film**

- **Chest CT**
  Greater sensitivity for differences in radiographic density than CXR

- **Nuclear Medicine Studies**
  *Gallium or FDG scanning* – can be used to differentiate fibrosis from viable tumor or infection, but cannot distinguish between infection and tumor; not routinely used.
Characteristic Radiologic Findings

Early Findings (1 to 6 months)

1) **Sharp, well-defined edges which cross normal tissue boundaries**
   Linear edge corresponds to radiation port

2) **Consolidation of parenchyma**
   CXR – patchy or confluent
   CT – homogeneous or patchy consolidation

3) **Volume loss**
   Secondary to plugging, decreased surfactant

4) **Air bronchograms on CXR**
   Major and segmental bronchi rarely affected

Note: Occasionally changes may occur outside radiation field, rarely in contralateral lung
Characteristic Radiologic Findings

Late Findings (6 or more months)

1) Alteration of normal thoracic architecture
   Shifting of mediastinum; elevation of hemidiaphragm; shifting of hila; adhesions among pleura, pericardium, diaphragm

2) Fibrosis of parenchyma (in non-anatomic distribution)
   CXR – retraction
   CT – discrete or solid consolidation

3) Pleural effusion
4) Thickening of pleura
5) Pericardial effusion
6) Bronchiectasis

Note: Occasionally changes may occur outside radiation field, rarely in contralateral lung
Normal Anatomy: Lung

Because failure to respect normal tissue boundaries is a key feature of radiation injury, it is helpful to review normal lung anatomy. The lungs are divided into lobes (3 on the right, 2 on the left). Each lobe is further subdivided into segments based on bronchial branches (10 on the right, 8 on the left).
Normal Anatomy: Lung

Because failure to respect normal tissue boundaries is a key feature of radiation injury, it is helpful to review normal lung anatomy. The lungs are divided into lobes (3 on the right, 2 on the left). Each lobe is further subdivided into segments based on bronchial branches (10 on the right, 8 on the left).
Normal Anatomy: Lung

Fissures separating the lobes can be seen on CXR and CT. Fissures can also occur between the segments of the lung and are called accessory fissures.

Percentages indicate frequency fissure is seen on chest radiographs

Courtesy of James Busch, MD. BIDMC
Radiation Portals

Radiation portals are customized for each patient, depending on the size and location of the tumor. Shields are created to reduce exposure to uninvolved parenchyma. In lung CA, the supraclavicular nodes are usually included in the field to prevent mets.

1) Mass
2) Radiation port
3) Shields
Patient 2: Characteristic Findings: Early

Finding: "Evidence of left upper lobe volume loss"; slight superior shift of left hilum

Finding: Paramediastinal lung opacification with geographic margins

Note: Pt is status-post median sternotomy for resection of mediastinal mass
Patient 3: Characteristic Findings: Early/Late

**Finding**: Geographic configuration of interstitial opacities in right mid and lower lung zones

**Finding**: Elevation of right hemidiaphragm; volume loss in right lung
**Finding** Parenchymal opacities with linear edge. Consists of ground glass opacities, reticulation, and bronchiectasis. This is an example of “discrete consolidation”, in which changes occur within the portal but do not uniformly involve it.

**Finding**: Pleural effusion within area of treatment port (avg HU = 13.8, indicating fluid density)

**Finding**: Volume loss in right lung

1) Aorta  
2) Left Atrium  
* Mass/Consolidation
Patient 5: Characteristic Findings: Late

**Finding**: Slight deviation of trachea, suggesting mild mediastinal shift

**Finding**: Elevation and tenting of right hemidiaphragm. Adhesions between pleura and diaphragm

**Finding**: Contracture and volume loss of right lower lobe

**Finding**: Opacification of middle fissure, slight inferior displacement
Patient 5: Characteristic Findings: Late

Finding
Elevation and tenting of right hemidiaphragm. Adhesions between pleura and diaphragm

Lateral view of previous chest film
Patient 6: Characteristic Findings: Late

Finding: Parenchymal opacification in left lung with a linear lateral margin, consistent with edge of radiation port

Finding: Evolving traction bronchiectasis, consistent with fibrosis. Example of “solid consolidation”, in which entire treated area is involved with associated bronchiectasis

Finding: Pleural effusion within area of treatment port (avg HU = 15, indicating fluid density)

1) Aorta
2) Right Pulmonary Artery

Finding: Volume loss in left lung

Note: Pt is status-post resection of mediastinal mass
Diff Dx of Radiation-Induced Lung Injury

- Recurrent Neoplasm
- Lymphangitic Spread of Neoplasm
- Infection
  - Bacterial
  - Viral
  - Fungal
- Chemical Pneumonitis
  - Inhalation exposures
  - Chemotherapy-induced
Distinguishing Among Diff Dx

Criteria favoring alternate diagnoses

**Neoplasm**
- More than 4 months between XRT and disease manifestation
- Presence of metastases
- Progression of radiographic abnormalities and sx
- Changes occur outside radiation field
- Hemoptysis

**Lymphatic Spread of Neoplasm**
- Prominent change in lung base associated with septal lines

**Infection**
- Positive cultures
- Lobar or anatomic distribution
- Persistent high fever
The geographic opacification suggests our patient has post-radiation fibrosis. The diffuse ground glass opacification is concerning for atypical infection or drug toxicity given its location outside the treatment port. Bronchoscopy was performed, and negative biopsies ruled out lymphagitic spread of cancer. Our patient was treated with 7-days of ABX with some improvement, but went on to develop significant radiation fibrosis.
Summary

We discussed:

- **The Radiologic Work-up of Solitary Pulmonary Nodule**

- **Review of Normal Lung Anatomy**

- **Description of Radiation-Induced Lung Injury**
  - Pathogenesis and Clinical Manifestations
  - Menu of Tests
  - Characteristic Radiologic Findings: Most importantly, the failure to respect normal anatomic boundaries
  - Differential Diagnosis of Radiation-Induced Lung Injury, emphasizing the importance of considering the radiologic findings in conjunction with the clinical history and presentation
References


8) Lasky J, Merrill W. “Radiation-Induced Lung Injury”. www.uptodate.com

9) Lecture by James Busch, MD
Acknowledgements

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