OFF THE BEATEN TRACK:
A Pictorial Review of Atypical Features of Pulmonary Metastases

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INTRODUCTION

• Extrathoracic malignancies have a marked predilection for metastasizing to the lung parenchyma
  • 20-54% of patients with solid tumors have pulmonary metastases at autopsy

• Numerous pathways for metastatic spread to the lungs exist, allowing for a wide array of imaging findings
  • Tumor cells can access the lungs via:
    • Pulmonary/bronchial vessels
    • Lymphatics
    • Airways
    • Direct invasion from adjacent neoplasia

• Chest CT is the gold standard for the diagnosis of pulmonary metastases
INTRODUCTION

• Many malignancies present with **TYPICAL** radiologic findings of metastatic disease to the chest:
  
  1. Multiple peripherally located round nodules
     • Hematogenous spread
  2. Thickening and nodularity of the interstitium
     • Lymphangitic carcinomatosis

• However, metastases can display **ATYPICAL** imaging features that overlap with findings of common nonmalignant conditions
  
  • Familiarity with these atypical presentations is prudent to avoid discarding metastatic lesions as benign
LEARNING OBJECTIVES

- Identify typical and atypical imaging features of pulmonary metastases.
- Review the main mechanisms of tumor spread to the lungs and the underlying pathophysiology of the atypical imaging features.
- Recognize the most common primary malignancies that result in the various patterns of pulmonary metastases.
- Briefly evaluate the common nonmalignant diseases that atypical metastases mimic.
TYPICAL IMAGING PATTERNS
1. HEMATOGENOUS METASTASES

- Most common pattern of metastatic dissemination to the lungs
- Seen in malignancies affecting organs that have venous drainage directly to the lungs:
  - Thyroid
  - Adrenals
  - Kidneys
  - Testes
  - Head and neck
  - Skin (Melanoma)
  - Bones (Osteosarcoma)

- IMAGING: Multiple solid nodules
  - Well circumscribed
  - Spherical
  - Lower/mid lungs
  - Random distribution
  - Variable size
    - **A. MILIARY**: 1-3mm
    - **B. CANNONBALL**: >5cm

70-year-old female with metastatic sarcoma. Innumerable spherical lower/mid lung predominant solid pulmonary metastases.
1A: MILIARY METASTASES

• MOST COMMON PRIMARIES:
  • Hypervascular tumors
    • Thyroid carcinoma
    • Melanoma
    • Renal cell carcinoma
    • Ovarian carcinoma

46-year-old female with metastatic papillary thyroid cancer. Innumerable mid and lower lung predominant 1-3mm solid pulmonary nodules with increased FDG avidity.
1B: CANNONBALL METASTASES

• MOST COMMON PRIMARIES:
  • Colorectal carcinoma
  • Renal cell carcinoma
  • Melanoma
  • Testicular carcinoma
  • Endometrial sarcoma

59-year-old female with endometrial sarcoma presents with shortness of breath. Multiple large (several >5cm), well circumscribed, spherical, solid cannonball metastases on chest radiograph and chest CT.
2. LYMPHANGITIC CARCINOMATOSIS

• PATHOPHYSIOLOGY:
  • POSSIBLE MECHANISMS OF LYMPHANGITIC DISSEMINATION:
    • 1. Direct infiltration via metastatic mediastinal/hilar nodes
    • 2. Indirect dissemination via a hematogenous route with subsequent lymphatic invasion
  • Pathologically observed in 56% of patients with metastatic disease
    • However, radiographic findings are not as prevailing

• MOST COMMON PRIMARIES:
  • Adenocarcinoma (80%): breast, gastric, pancreatic

81-year-old male with metastatic adenocarcinoma. Chest CT: multiple solid pulmonary nodules with left upper lobe predominant septal thickening consistent with local lymphangitic carcinomatosis.
2. LYMPHANGITIC CARCINOMATOSIS

**IMAGING:**
- Beaded, nodular, or smooth interlobular septal thickening
- +/- Thickening of bronchovascular bundles
- No distortion of lung parenchyma
- +/- Lymphadenopathy (50%)
- +/- Pleural effusions

**DDX:**
- Sarcoidosis:
  - No pleural effusions
  - +/- Calcified lymphadenopathy
- Pulmonary edema:
  - Smooth septal thickening
  - +/- Cardiomegaly
  - + Pleural effusions
  - Gravity dependent findings
  - Resolution with diuretics
- Pulmonary fibrosis:
  - Architectural distortion
  - Often slowly progressive
- Lymphoproliferative diseases

61-year-old female with metastatic breast adenocarcinoma. 
**Chest CT:** Ground glass opacities and irregular septal thickening consistent with lymphangitic carcinomatosis.
ATYPICAL IMAGING FEATURES
1. CALCIFICATION

- POSSIBLE PATHOPHYSIOLOGIC MECHANISMS OF CALCIFICATION:
  1. Bone formation in tumor osteoid
  2. Ossification of tumor cartilage
  3. Calcification deposited in damaged tissue
  4. Mucoid calcification

- MOST COMMON PRIMARIES:
  - Sarcomas:
    - Osteosarcoma
    - Chondrosarcoma
    - Synovial sarcoma
  - Mucinous carcinomas:
    - Colon carcinoma
    - Ovarian carcinoma
    - Breast carcinoma
  - Medullary thyroid carcinoma

70-year-old female with metastatic ovarian cancer.
Chest CT: Large metastatic pulmonary nodules with mucoid calcification.
1. CALCIFICATION

• Nodule calcification patterns:
  - BENIGN:
  - Diffuse
  - Central (if encompassing >50% of the nodule)
  - Popcorn
  - Laminated
  - MALIGNANT:
  - Stippled
  - Eccentric

• DDX OF CALCIFIED NODULE(S):
  - Granulomatous disease
    - Multiple nodules with benign patterns of calcification
    - Associated calcified lymphadenopathy and/or hepatosplenic calcified granulomas
  - Hamartoma
    - Fat attenuation
    - Popcorn calcification
    - Often only a single lesion
  - Carcinoid
    - Commonly involves a bronchus/bronchiole with post obstructive atelectasis or pneumonia

20-year-old male with history of osteosarcoma.
*Surveillance CT 2 years post Dx: new RLL pulmonary nodule with eccentric calcification.
Surgical excision pathology consistent with osteosarcoma.

*Surveillance CT 3.5 years post Dx:
New eccentrically calcified RLL pulmonary nodule consistent with a new metastasis.
2. CYSTIC METASTASES

• POSSIBLE PATHOPHYSIOLOGIC MECHANISMS OF CYST FORMATION:
  1. Cancer cells infiltrate alveolar walls, destroy septa, and form cysts (similar to emphysema)
  2. Infiltration of cancer cells into the walls of pre-existing benign bullae
  3. Check valve mechanism: cells obstruct bronchioles which then dilate and appear cystic

• MOST COMMON PRIMARIES:
  • Soft tissue sarcomas
  • Rectal carcinoma
  • Lung adenocarcinoma
  • Cellular fibrous histiocytic tumors

64-year-old female with pancreatic adenocarcinoma and no distant metastases was treated with Whipple procedure and chemotherapy.

Rising CA 19-9 four years post surgery.

SURVEILLANCE CHEST CT:
New air cysts with thin walls consistent with metastatic disease. No solid nodules.
2. CYSTIC METASTASES

• IMAGING:
  • Multiple well defined air or fluid filled cysts with thin perceptible walls (<3mm)

• DDX OF AIR FILLED CYSTS:
  • Cavitary lesion: Irregular, thick walls
  • Pulmonary Langerhans cell histiocytosis
    • Upper/mid lung predominant, spares bases
    • Variable sized bizarre shaped cysts, +/- small nodules
  • Lymphocytic interstitial pneumonia
    • +/- Ground glass opacities and centrilobular nodules
  • Lymphangioleiomyomatosis:
    • Exclusively in females
    • Diffuse cysts
  • Birt-Hogg-Dubé Syndrome
    • Renal neoplasm
    • Skin fibrofolliculomas
    • Cysts few in number

30-year-old male with hemoptysis. Multiple bilateral masses on chest radiograph. CT chest abdomen pelvis shows multiple fluid filled cysts with thin perceptible walls. Additional findings of gynecomastia and a scrotal hydrocele (not shown).

DX: NONSEMINOMATOUS TESTICULAR CA
3. CAVITATION

- POSSIBLE PATHOPHYSIOLOGIC MECHANISMS OF CAVITATION:
  1. Central tumor necrosis from outgrowth or invasion/thrombosis of the blood supply
  2. Tumor infiltration erodes bronchiolar walls, obstructs the bronchus, and creates a cavity-like appearance via a check valve mechanism

- MOST COMMON PRIMARIES:
  - Squamous cell carcinoma: accounts for 69% of cavitary metastases
    - Head and neck
    - GU tract—especially in women
  - Adenocarcinoma—GI tract, breast
  - Sarcoma

16-year-old male with right neck/oropharyngeal undifferentiated teratocarcinosarcoma with metastatic disease in the left neck soft tissues. S/p surgical excision and chemotherapy.

Chest CT and PETCT 3 months post surgery: FDG avid thick walled cystic lesions in the right lung consistent with cavitary pulmonary metastases. Incidental note of lumbar spine FDG avid metastasis.
3. CAVITATION

**IMAGING:**
- Multiple nodules
  - Upper lobe and peripheral predominant
  - Variable sizes/shapes, **thick walls**
    - Thin walls: seen in adenocarcinomas and sarcomas

**DDX:**
- Primary lung malignancy
  - Overall more common to be cavitary than a metastasis
  - Single lesion with a thick and sometimes nodular wall
  - +/- Regional lymphadenopathy
- Septic emboli
  - Nodules evolve/cavitate quickly
  - Acutely ill patient
- Granulomatosis with polyangiitis
  - +/- Subglottic stenosis
  - +/- Pulmonary hemorrhage
  - History of sinus and renal disease
- Tuberculosis
- Lung abscess

79-year-old male with high grade urothelial (transitional cell) carcinoma. **Chest CT:** multiple peripheral, irregular, thick walled cavitary lesions consistent with metastatic disease.
4. ENDOBRONCHIAL METASTASES

- POSSIBLE PATHOPHYSIOLOGIC MECHANISMS:
  1. Tumor implant on bronchial wall via aspiration, lymphatic dissemination, or hematogenous spread
  2. Malignant cells surrounding bronchus invade the bronchial wall and form an intraluminal lesion

- MOST COMMON PRIMARIES:
  - Renal cell carcinoma
  - Melanoma
  - Lymphoma
  - Breast carcinoma
  - Colon carcinoma

50-year-old female with adrenal cortical carcinoma. Surveillance chest CT: endobronchial tumor in the center of the bronchus intermedius and a 6 x 3cm right middle lobe metastasis. Multiple additional bilateral solid pulmonary nodules are present (not shown).
4. ENDOBRONCHIAL METASTASES

• **IMAGING:**
  - Endobronchial nodule or mass
  - Post obstructive atelectasis, mucoid impaction, or pneumonitis
  - Tree in bud opacities

• **DDX:**
  - Bronchogenic carcinoma
  - Mucus plugging
    - Patient Hx of chronic lung disease
    - Clearance/shifting on subsequent CT
  - Carcinoid
    - +/- Calcifications
    - Hypervascular

48-year-old male with colon adenocarcinoma. Chest CT: bilateral bronchial wall thickening, bronchial wall nodularity, and a 24mm left lower lobe mass with endobronchial extension.
5. TUMOR EMBOLI

• PATHOPHYSIOLOGY:
  - Emboli are intravascular metastases *without* an extravascular component
  - Microvascular invasion by tumor cells causes vascular obstruction and pulmonary hypertension
  - Microscopically present at autopsy in up to 26% of patients with solid tumors

• CLINICAL:
  - Progressive cor pulmonale with dyspnea and signs of elevated pulmonary pressures (ascites, peripheral edema)
  - Overall poor prognosis: Mean survival time is 4-12 weeks after onset of symptoms

• MOST COMMON PRIMARIES:
  - CARCINOMAS:
    - Hepatocellular
    - Breast
    - Renal cell
    - Gastric
    - Prostate
    - Choriocarcinoma
5. TUMOR EMBOLI

• IMAGING:
  • CTA:
    • Multifocal dilation, beading, and pruning of peripheral subsegmental arteries
    • Enhancing intravascular filling defects
    • Peripheral wedge shaped opacities from pulmonary infarction
    • +/- Tree in bud pattern with tumor filling the centrilobular arteries
  • VQ Scan:
    • Numerous peripheral subsegmental perfusion defects with normal ventilation

• DDX:
  • Pulmonary thromboembolism: usually indistinguishable
    • Arterial dilation is less common
    • Resolves with anticoagulation
  • Pulmonary artery sarcoma
    • Often a single large central filling defect
5. TUMOR EMBOLI

25-year-old female status post surgical excision of a high grade spindle cell sarcoma presents 8 mo later with recurrence at the surgical site (thigh) and shortness of breath. CT chest MIP and soft tissue window images demonstrate beaded dilation and abrupt pruning of multiple bilateral subsegmental arteries consistent with tumor emboli.

Dual energy imaging: Multiple peripheral subsegmental perfusion abnormalities.

Left lower lobe peripheral wedge shaped consolidation consistent with a pulmonary infarct.
6. SPONTANEOUS PNEUMOTHORAX

• POSSIBLE PATHOPHYSIOLOGIC MECHANISMS:

  1. Necrosis and/or rupture of a peripheral cavitary/cystic metastasis with involvement of the pleura, thus creating a bronchopleural fistula
  2. Metastasis obstructs a bronchiole leading to overdistension and rupture

• MOST COMMON PRIMARIES:

  • Seen in aggressive tumors that are prone to necrose and in metastases with chemotherapy-induced necrosis
  • SARCOMAS: osteosarcoma, angiosarcoma
    - 5-7% of osteosarcoma metastases cause a pneumothorax

• DDX:

  • Emphysematous bleb/bulla rupture

76-year-old male with adenocarcinoma presents with acute chest pain. Chest CT: Large right pneumothorax, multiple solid and cystic pulmonary metastases.
7. PERILESIONAL HEMORRHAGE

**PATHOPHYSIOLOGY:**
- Hypervascular tumors contain fragile neovessels that are prone to thrombose/rupture

**IMAGING:**
- **CT Halo sign:** soft tissue nodule with surrounding ground glass attenuation

**MOST COMMON PRIMARIES:**
- Choriocarcinoma
- Angiosarcoma
- Renal cell carcinoma
- Melanoma

**DDX:**
- Angioinvasive aspergillosis
  - +/- Cavitary pulmonary nodules
  - Cough, fever, chills
- Granulomatosis with polyangiitis
  - Hx of sinus and renal disease
  - Nodules are less distinct
- Tuberculosis
- Bronchogenic adenocarcinoma

88-year-old male with high grade tibial epithelioid angiosarcoma status post curative surgical resection presents 2 years after diagnosis with hemoptysis.

Chest CT: Solid nodules with surrounding ground glass attenuation consistent with hemorrhagic metastases.
• Solitary pulmonary nodule detected on chest radiograph:
  • **LOW** probability (0.4-9%) of being a metastasis if there is no history of malignancy
  • **INTERMEDIATE** probability (25%) of being a metastasis in a patient with a history of an extrapulmonary malignancy
  • 90% are benign if <2cm

• MOST COMMON PRIMARIES:
  • Melanoma
  • Bone tumors
  • Soft tissue sarcoma
  • Testicular carcinoma
  • Colorectal carcinoma

20-year-old female with fibrolamellar hepatocellular carcinoma s/p resection.

Initial staging chest CT: negative for pulmonary nodules.

Surveillance chest CT 5 years after diagnosis: Solitary solid noncalcified nodule in the RLL consistent with biopsy proven hepatocellular carcinoma metastasis.
82-year-old male with facial melanoma presents 3 years post diagnosis with chest pain.

PETCT: Single FDG avid RUL mass (SUV 20.4) with no other findings of metastatic disease.

CHEST CT: Single solid noncalcified 3.3cm lobulated RUL mass consistent with biopsy proven high grade metastatic melanoma.

CHEST RADIOGRAPH: 3-4 cm right upper lobe mass.
8. SOLITARY METASTASIS

• **DDX:**
  - Primary lung cancer
    - More common than a solitary metastasis if patient has malignancy of the head and neck, urinary system, prostate, or uterus
    - More common if nodule is >2cm
    - Irregular spiculated borders
  - Carcinoid:
    - Hypervascular
    - +/- Calcification
  - Infection: granuloma, aspergilloma, etc
  - AVM:
    - Lower lobe and peripheral predominant
    - Feeding and draining vessels
  - Benign neoplasm: hamartoma, lipoma, etc
    - Fat density
    - +/- Calcification
  - Inflammatory: granulomatosis with polyangiitis, rheumatoid, sarcoid
    - Often multiple nodules
9. LEPIDIC GROWTH

• PATHOPHYSIOLOGY:
  • Tumor cells spread along intact alveolar walls
  • Tumor utilizes lung parenchyma as a scaffold without causing architectural distortion

• IMAGING:
  • Airspace nodules
  • Consolidation with air bronchograms
  • Focal or extensive ground glass opacities
  • Halo sign

• MOST COMMON PRIMARIES:
  • Adenocarcinomas
    • Gastrointestinal system especially pancreatic
    • Breast
    • Ovarian

• DDX:
  • Pneumonia
  • Angioinvasive aspergillosis
  • Granulomatosis with polyangiitis
  • Tuberculosis
  • Pulmonary adenocarcinoma

57-year-old male with pancreatic adenocarcinoma. Staging chest CT: Peripheral pulmonary consolidations with surrounding ground glass halo consistent with lepidic growth of metastatic adenocarcinoma.
70-year-old female with history of pancreatic adenocarcinoma presents 2 years after Whipple procedure with shortness of breath.

Chest CT: Extensive bilateral peripheral predominant solid and ground glass nodules consistent with lepidic growth of metastatic adenocarcinoma.
REFERENCES


CONTACT INFORMATION:

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