Complete Understanding of the Metastatic Lung Tumors: Basic and Applied Knowledge for Radiologists

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☑ THE ALL AUTHORS HAVE NO CONFLICT OF INTEREST TO DISCLOSE WITH RESPECT TO THIS PRESENTATION.
INTRODUCTION

Metastatic lung tumor is typically detected on CT as multiple peripherally located nodules with various sizes. However, it is sometimes difficult to differentiate from non-malignant tumors because of atypical CT findings: calcification, endobronchial spread, ground-glass opacity around nodules (halo sign), pneumothorax, lepidic growth pattern, and reversed halo sign.

The purpose of this exhibit is:

to review the typical and atypical radiological findings of metastatic lung tumors with making differential diagnoses.

calcification, endobronchial spread, ground-glass opacity around nodules (halo sign), pneumothorax, lepidic growth (Air space) pattern, and reversed halo sign.

PURPOSE OF THIS EXHIBIT

1. Radiological findings according to metastatic patterns or primary sites:
   a) Hematogenous metastasis
   b) Lymphatic metastasis
   c) Endobronchial metastasis

2. Metastases with atypical radiological findings:
   Calcification, Halo sign, Cavitation and Pneumothorax, Lepidic growth (Air space) pattern, and Reversed halo sign.
1. Hematogenous metastasis:

- Account for 30-50% in malignant lung tumors
- Tumor invades to veins. They spread through pulmonary artery. (Rarely through bronchial artery)

**Typical CT findings**
- Predominantly in lower lobe
- Predominantly in the periphery
- About 75%: multiple nodules (Random distribution)

Metastases can be seen sometimes as solitary nodule, cavitary nodule, minute nodule, and various patterns of nodules.

<table>
<thead>
<tr>
<th>Solitary nodule</th>
<th>From Renal cell carcinoma, Breast cancer, Bladder cancer, etc.</th>
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</thead>
<tbody>
<tr>
<td>Cavitary nodule</td>
<td>From Squamous cell cancer from head &amp; neck, uterine cervical cancer, Sarcoma, etc.</td>
</tr>
<tr>
<td>Minute nodule</td>
<td>From Thyroid cancer, Prostate cancer, etc.</td>
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</table>

A 61-year-old man underwent right nephrectomy for clear cell carcinoma. CT shows a solitary nodule with well-defined and lobulated margin. Metastases from renal cell carcinoma and hepatocellular carcinoma tend to have well-defined and lobulated margin. Pathological specimen shows that neoplastic cells contain fine granular acidophilic cytoplasm.

**Solitary metastasis from renal cell carcinoma**

**Rare case 1**

A 62-year-old man with papillary renal cell carcinoma

CT: a solitary nodule including a small amount of ground-glass opacity (GGO) with ill-defined margin and an air bronchiologram.

Pathological specimen: both hyperplasia of the alveolar epithelium and thickening of the alveolar septa without neoplastic cells.

GGO may correspond to both reactive hyperplasia of the alveolar epithelium and reactive thickening of the alveolar septa in the surrounding normal lung tissue.

(H&E, x1)

**Rare case 2**

A 63-year-old man with spindle renal cell carcinoma

CT: a solitary nodule including GGO with ill-defined margin, spiculations, air bronchiologram and pleural indentation.

Pathological specimen: neoplastic cells are present in both the inner and the outer of vessels.

GGO may correspond to neoplastic cells spreading in the alveolar septa with preservation of the alveolar airspace.

(H&E, x100)

Multiple metastases from colon cancer

57-year-old man

Faint calcifications
Multiple metastases from osteosarcoma

27-year-old man

Bone scintigraphy: Extra-osseous accumulation

Calcifications
Calcification or ossification can occur in metastatic nodules, and can also be seen in treated metastatic choriocarcinomas. Calcification is frequently confirmed only with CT.

### Characteristics of Calcification

<table>
<thead>
<tr>
<th>Calcification of metastatic tumors</th>
<th>Mechanism</th>
<th>Relevant tumors</th>
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<tbody>
<tr>
<td></td>
<td>Bone formation</td>
<td>Osteosarcoma</td>
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<td></td>
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<td>Chondrosarcoma</td>
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<td></td>
<td>Dystrophic calcification</td>
<td>Thyroid cancer (Papillary carcinoma)</td>
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<td></td>
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<td>Giant cell tumor (Bone)</td>
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<td></td>
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<td>Synovialsarcoma</td>
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<td>Post-treatment of metastatic tumor</td>
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<td></td>
<td>Mucoid calcification</td>
<td>Mucous-producing adenocarinoma derived from gastrointestinal tract, mammary gland, and ovary</td>
</tr>
</tbody>
</table>

**Suspected benignancy**
- Diffuse
- Laminated
- Central nodular
- Popcornlike

**Suspected malignancy**
- Eccentric
- Stippled

Fat density is useful for the diagnosis of Pulmonary Hamartoma.

A 68-year-old man presented with popcornlike calcification.

Popcornlike calcification is one of the famous findings, but its frequency accounts for about 30%.

No calcification and fat density were also observed.
The mechanism of calcification may be due to the engulfing calcified granuloma.

Relatively high FDG uptake

Diagnosis:
Large cell carcinoma
Other diseases with multiple pulmonary nodules

Amyloidosis is a heterogeneous group of diseases characterized by extracellular deposition of insoluble fibrillar proteins that aggregate in a β-pleated sheet configuration.

A 65-year-old woman with SjS

Three types

1. Nodular type
   * Solitary or multiple nodules < 5 cm in diameter
   * With round, lobular, irregular margin
   * Often in periphery or just below pleura
   * Calcification: 30 - 50%

2. Tracheobronchial type
   * Submucosal deposition of amyloid in the trachea and segmental airways
   * Often with bronchial wall thickening and luminal narrowing

3. Diffuse type
   * Reticulation, interlobular septal thickening
   * Scattered micronodules with 2–4 mm in diameter

The tracheobronchial and diffuse types have a poorer prognosis than nodular type.
Epithelioid hemangioendothelioma (EHE) of the lungs is a neoplasm with a vascular line of differentiation.

EHE represents an intermediate-grade, malignant, mesenchymal neoplasm with a characteristic histological appearance and immunohistochemical profile.

CT findings:
- Often multiple nodules with well-defined Margin.
- Beaded appearance due fusion or contact in a cord-like structure.
- Cavitary and calcification are uncommon.

Other diseases with multiple pulmonary nodules-2:

1. Radiological findings according to metastatic patterns or primary sites:
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   c) Endobronchial metastasis

2. Metastases with atypical radiological findings:
   - Calcification, Halo sign, Cavitation and Pneumothorax, Lepidic growth (Air space) pattern, and Reversed halo sign.

   Beaded appearance due fusion or contact in a cord-like structure.

   Cavitary and calcification are uncommon.

http://pulmonary.exblog.jp/12508993/
In most cases, lymphangitic carcinomatosis progresses rapidly and patients deteriorate, however in some cases changes may remain stable over considerable time.

CT findings

- Subpleural nodules
- Often nodular and irregular interlobular septal thickening
- Relatively little destruction of overall lung architecture
**Lymphangitic carcinomatosis**

**Mechanism**

- Spread into the lymphatics usually occurs following haematogenenous seeding of the lungs, with subsequent lymphatic involvement.
- It may also occur by retrograde spread into lymphatics from the mediastinal and hilar lymph nodes.

**Tumor:**

Both within lymphatics and in the adjacent interstitium. Distribution of tumors is asymmetric and patchy. It is usually bilateral but may be unilateral.
Please pay your attention to the red square.

In WHO2015, **intravascular large B cell lymphoma** and **Erdheim–Chester disease** are newly added as lung tumors.
Erdheim–Chester disease (ECD)

Erdheim–Chester disease is one of the lymphoproliferative disorders.

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about 20% of patients

A 75-year-old woman with colon cancer

**Endobronchial Metastasis**

- The frequency is low: only 2% of cases in the major airway.
- The common sources are kidney, breast, and colorectal cancers.
- Endobronchial lesion ⇒ An atelectasis of a lobe or the entire unilateral lung.

* In many cases, it is difficult to differentiate among:
  endobronchial metastasis, a primary bronchogenic carcinoma, and other tumors

**Two possible routes for the pathogenesis**

(a) A metastasis can occur directly on the bronchial wall:
  aspiration of tumor cells, lymphatic spread, or hematogenous metastasis to the bronchial wall.
(b) Tumor cells in the lymph nodes or lung parenchyma that surround the bronchus grow along the bronchial tree.

was confirmed as endobronchial metastasis by biopsy.

A 85-year-old man with colon cancer

Intrabronchial soft tissue with enhancement can be seen. This case was confirmed as a large cell carcinoma by surgery.
A 93-year-old man

Endobronchial carcinoid in adults are rare (<1% of all lung cancers) but are the most common intrabronchial tumor in children. Patients have often obstructive symptom such as cough, wheezing. In primary pulmonary carcinoid, carcinoid syndrome is extremely rare because there is rich serotonin degrading enzyme in lung.

Typical CT finding: Intrabronchial tumor with smooth margin and sometimes with eccentric calcification. Tumor is strongly enhanced.

Carcinoid syndrome: characterized by flushing, palpitations, wheezing, shortness of breath, and diarrhea which are caused by serotonin release from the tumor.

A 67-year-old woman after surgery of ovarian cancer

We can see a peripheral nodule with irregular margin in rt. middle lobe. We can see also a dilated air space in the periphery. About 10 months after surgery, the size of nodule is larger, and obstructive change is strong. This case was confirmed as an atypical carcinoid.
Atypical carcinoid

* Larger size than typical carcinoid
* Irregular margin
* Inhomogeneous density
* Often in the periphery
* Tendency to spread to lymphnodes
1. Radiological findings according to metastatic patterns or primary sites:
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2. Metastases with atypical radiological findings:
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A 71-year-old man with colon cancer

Air-space pattern
Air

Metastases from an adenocarcinoma may spread into the lung along the intact alveolar walls (lepidic growth), in a fashion similar to an invasive mucinous adenocarcinoma. Adenocarcinomas from the breast, ovary, and colon can show this pattern of metastasis.

D/D: Pneumonia, Invasive mucinous adenocarcinoma


Invasive mucinous adenocarcinoma (primary lung cancer) appears to be a pneumonia.
A 27-year-old man with cardiac angiosarcoma

Hemorrhage around nodules

CT finding is a nodular attenuation surrounded by a halo of ground-glass opacity (CT halo sign).

Angiosarcomas and choriocarcinomas are the most representative causes of hemorrhagic metastases.

Fragility of the neovascular tissue that leads to a rupture of the vessel is a probable cause for hemorrhage.

D/D: fungus infection, granulomatosis with polyangitis (Wegener granulomatosis), lung cancer, e.t.c.

A 39-year-old man with synovial sarcoma in left thigh.

Subpleural cavitary nodule can be seen in left lower lobe.

2 months later

After 2 months, this nodule is larger, and pneumothorax can be seen newly in the opposite lung. A cause of pneumothorax may be due to a rupture of subpleural minute metastases in right middle lobe.
Characteristics of metastases from sarcoma

The frequency of a pneumothorax in a patient with an osteosarcoma has been reported to be approximately 5%–7%.

A spontaneous pneumothorax in a patient with a sarcoma

the possibility of occult pulmonary metastases

Some nodules appear to have reversed halo sign.

Metastasis from pancreatic cancer

- Nodules with irregular margin
- Lepidic pattern

Atypical patterns can be seen.
Another case:
Pulmonary metastases from pancreatic cancer

A 62-year-old man with pancreatic cancer with FDG uptake (SUVmax: 4.5) has nodules or ground-glass opacities with ill-defined border that can be seen. Subpleural nodules can also be seen. This case is atypical pulmonary metastases due to hematogenous and lymphatic metastases from pancreatic cancer.

Nodules or ground-glass opacities with ill-defined border can be seen. Subpleural nodules can be also seen. This case is atypical pulmonary metastases due to hematogenous and lymphatic metastases from pancreatic cancer.
**Pulmonary tumor thrombotic microangiopathy (PTTM)**

A 84-year-old woman with hepatocellular carcinoma

**Metastatic tumor cells:**
1. Occlude small pulmonary arteries
2. Induce microthrombosis and fibrocellular intimal proliferation by activating a coagulation cascade and inflammatory mediators.

**Diffuse narrowing and occlusion of the small pulmonary arteries:**
Secondary pulmonary hypertension

**Representative causes:** gastric cancer
(Rare causes; lung, breast, esophageal, gallbladder, colon, pancreatic, liver, ureteral, urinary bladder, and ovarian cancer)

**Representative histological tumor type:** adenocarcinoma

**CT findings of PTTM are Non-specific**
consolidation, diffuse ground-glass opacity, small nodules, a tree-in-bud appearance, interlobular septal thickening, centrilobular ground glass opacities, Reticular nodular opacities, and cavitation

Contrast-enhanced CT shows an increase in the diameter of the main pulmonary artery without filling defects. Thin-section shows diffuse GGO predominantly in the peripheral lung regions. Focal consolidation and nodular opacities are also seen in the periphery.

Adenocarcinoma cells embolizing small pulmonary arteries with fibrocellular intimal proliferation.

DT = (t × log 2)/log(Vt/Vi)

DT: doubling time
t: time interval between CT examinations
Vi: initial volume, Vt: final volume

Case 1: Solid nodule with 8mm in diameter

After 72 days
325mm³ → 337mm³
Doubling time: 1376 days
Diagnosis: Hamartoma

Case 2: Solid nodule with 8mm in diameter

After 21 days
319mm³ → 357mm³
Doubling time: 129 days
Diagnosis: Metastasis from parotid cancer

DT: 20 - 400 days in most malignant tumors

DT: 100 days in typical malignant tumors
Mass is originally based on the previous paper (Mull RT. AJR 1984;143:1101-1104).

Mass is defined as follows:

\[ \text{Mass} = \text{volume} \times (\text{CT number} + 1000) \]

Mass measurements have the smallest measurement variability compared to the diameter and volume measurements. Mass measurement allowed earliest detection of growth in malignant nodules. Mass measurement is one of the indicators for quantification of change in nodule density over time.

**Change in nodule density over time**

- **GGN**
  - Volume: 153 mm³
  - Mean CT value: -715 HU
  - Mass: 48.65 mg

- **Part-solid**
  - Volume: 164 mm³
  - Mean CT value: -642 HU
  - Mass: 58.72 mg

- **Solid**
  - Volume: 80 mm³
  - Mean CT value: -552 HU
  - Mass: 91.39 mg

We can see almost no change of size despite an increase in density on CT images: GGN → part-solid → Solid. This nodule was diagnosed as adenocarcinoma after surgery. **Mass** may be useful for the quantification of change in nodule density over time.

Although it is difficult to diagnose metastases with atypical CT findings, a solid understanding of various CT findings in metastatic lung tumors based on metastatic patterns or primary sites is of great importance and may contribute to the differentiation from other non-malignant pulmonary diseases.

Thank you for your attention!

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