Uncommon Lung Tumors: Radiologic-pathologic correlation

Exhibit Category: Thoracic Neoplasms

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Learning Objective/Outcomes

- To review the rare lung tumors based on the 2015 World Health Organization (WHO) classification of tumors of the lungs
- To illustrate the radiologic features of the rare lung tumors on CT and PET/CT
- To correlate radiologic features of the rare lung tumors with histologic and genetic features
2015 WHO Classification of Lung Tumors

- Different approach to lung adenocarcinomas as proposed by the 2011 IASLC/ATS/ERS classification
- Updates on other rare histologic subtypes of lung tumors
  - changing the term sclerosing hemangioma to sclerosing pneumocytoma
  - adding NUT carcinoma
  - creating a group of PEComatous tumors
  - adding myoepithelioma and myoepithelial carcinoma
  - Other uncommon tumors: colloid adenocarcinoma, enteric adenocarcinoma, sarcomatoid carcinoma, intravascular lymphomatosis, etc.
Major changes in 2015 WHO classification of lung adenocarcinomas

1) Discontinuing the terms bronchioloalveolar carcinoma and mixed subtype adenocarcinoma
2) Adding Adenocarcinoma-in-situ to the list of pre-invasive lesions
3) Introducing the concept of minimally-invasive adenocarcinoma
4) Classification of invasive adenocarcinomas based on the predominant subtype
5) Use of the term “lepidic” for non-invasive component in an invasive adenocarcinoma
6) Introduction of the term “invasive mucinous adenocarcinoma” for cases previously classified as mucinous bronchioloalveolar carcinoma;
7) Discontinuing the use of clear cell and signet ring cell adenocarcinoma subtypes
8) Discontinuing the term mucinous cystadenocarcinoma and including them in colloid adenocarcinoma.
CONTENTS

◆ Epithelial tumors
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  ✓ Sarcomatoid carcinomas: pleomorphic, spindle cell, giant cell, carcinosarcoma
  ✓ Unclassified: Lymphoepithelioma-like carcinoma
  ✓ Salivary gland type tumors: epithelial-myoepithelia carcinoma
  ✓ Adenomas: sclerosing pneumocytoma
  ✓ Papillomas: glandular papilloma

◆ Mesenchymal tumors
  ✓ PEComatous tumors: lymphangioleiomyomatosis, PEComa
  ✓ Diffuse pulmonary lymphangiomatosis
  ✓ Inflammatory myofibroblastic tumor
  ✓ Epithelioid hemangioendothelioma
  ✓ Synovial sarcoma
  ✓ Pulmonary artery intimal sarcoma

◆ Lymphohistiocytic tumors
  ✓ MALT lymphoma
  ✓ Intravascular large B cell lymphoma
  ✓ Pulmonary Langerhans cell histiocytosis
Colloid adenocarcinoma has abundant extracellular mucin, which corresponds to homogeneous low-attenuation on contrast CT and low SUV on FDG-PET. Gross specimen shows soft, gelatinous, well-circumscribed nodule (bottom left). Note floating tumor cells in the mucin (arrows in bottom center).
CT shows well-circumscribed solid mass with lobulated contour and *poor contrast-enhancement*, which is correlated with abundant extracellular mucin. Low FDG-avidity is noted on PET/CT.

**Histology** shows *abundant extracellular mucin* (arrows) with floating tumor cells. 2015 WHO classification discontinues the term mucinous cystadenocarcinoma and include them in colloid adenocarcinoma.
Fetal adenocarcinoma with fetal pseudoglandular and canalicular period. Fetal adenocarcinoma is an adenocarcinoma resembling fetal lung (bottom right). The lesions usually present as a solitary, well-demarcated solid mass with variable contrast-enhancement on CT.
Enteric adenocarcinoma strongly resembles to colorectal adenocarcinomas, and the diagnosis of enteric adenocarcinoma needs exclusion of enteric primary in the GI tract.

**IHC profile:** positive for enteric markers (CDX-2, MUC2 and CK20) as well as lung markers (CK7 and TTF-1, etc).
Pleomorphic carcinoma (PC) is a poorly differentiated NSCLC that contains *more than 10% spindle and/or giant cells* or a carcinoma consisting only spindle or giant cells. There is strong association with *smoking*. This tumor shows very *aggressive behavior* and early postoperative recurrence.

**Imaging:** PC typically presents as a large necrotic mass (arrows) in upper lobe with chest wall invasion.

**Histology:** Spindle cell and giant cell tumors with some adenocarcinoma components (arrowheads)
Spindle cell carcinoma is a subtype of sarcomatoid carcinoma and consists of an almost pure populations of epithelial spindle cells, with no differentiated carcinomatous elements. 

**Imaging:** This tumor presents as a large peripheral mass, usually in upper lobes, showing central low attenuation (arrowhead), strong FDG uptake on PET, and frequently invasion to adjacent pleura. Spindle cell carcinomas are very aggressive tumors; distant metastases including unusual locations (arrow) (e.g: GI tract) are common.
Lymphoepithelioma-like carcinoma is a rare and distinctive tumor characterized by poorly differentiated morphology admixed with marked lymphocyte infiltrate and the presence of EBV in the nuclei of neoplastic cells. It is rare (0.9% of all lung cancer) and more common in South-East Asia. It affects non-smoking, young patients, and mostly women.

**Imaging and Histology:** As we can see from the pushing border (arrows) of the tumor, this tumor is expected to present as a well-defined solid mass on CT. Lymphoepithelioma-like carcinoma is characterized by a syncytial growth pattern, large vesicular nuclei, and heavy lymphocyte infiltration (right bottom).
Epithelial-myoepithelial carcinoma is a low-grade malignant epithelial tumor with biphasic morphology, inner layer of duct-like structures (arrowheads) and surrounding layer of myoepithelial cells. This tumor typically presents as a central endobronchial mass (arrows). Prognosis is usually excellent after curative resection.
Sclerosing pneumocytoma (SP) is a tumor of pneumocyte origin with a combination of histologic findings, including solid, papillary, sclerotic and hemorrhagic regions. It has a striking female predominance and is more common in Asian populations.

**Imaging and histology:** SP typically presents as a solitary well-defined mass with marked contrast-enhancement corresponding to the area of solid or papillary component. Sharply marginated low-attenuation corresponds to the area of hemorrhagic region (arrows).

Several microscopic patterns can be seen in a single lesion. Papillary component (left) and hemorrhagic region (right) are clearly visible on both gross and low-power microscopic examination.
Glandular papilloma (GP) is a benign papillary tumor lined by ciliated or non-ciliated columnar cells, with varying numbers of cuboidal and goblet cells. GP has excellent prognosis and malignant transformation has not been reported.

**Imaging and Histology:** Most GP present as an *endobronchial lesion*, but it GP may be incidentally detected as a *SPN* on screening CT. FDG avidity has been reported. Macroscopy shows central dilated bronchus (arrow) suggesting the *bronchial origin* of the tumor. Uniform columnar cells are admixed with mucinous cells.
PEComatous tumors arise from *Perivascular Epithelial Cells* and can present in the lungs in following forms: 1) lymphangioleiomyomatosis (LAM); 2) PEComa; 3) PEComatosis –with overlapping features between LAM and PEComa.

**CT:** Localized PEComas usually present as well circumscribed peripheral nodule/mass ranging 2-6cm. Note dense calcification (arrows)

**Pathology:** PEComas comprise rounded or oval cells with distinct borders and abundant clear or eosinophilic cytoplasm (arrows).
CT and histology: Multiple thin-walled cysts (LAM, red boxes) are randomly distributed in both lungs. Small solid nodules (arrows and blue box) are multifocal micronodular pneumocyte hyperplasias (MMPHs), which are often accompanied by tuberous sclerosis complex.
Diffuse pulmonary lymphangiomatosis is a diffuse proliferation of lymphatic spaces and smooth muscle along otherwise normal lymphatic vessels of the lungs, pleura and mediastinum. It is typically diagnosed shortly after birth or during childhood or young adulthood, with typically worsening dyspnea or chylous effusion. Prognosis is poor and lung transplantation is considered the last treatment.

**Imaging:** CXR shows diffuse *increased interstitial markings* and pleural effusion (left). CT shows diffuse and smooth *thickening of interlobular septa* and *peribronchovascular bundles*, mediastinal soft tissue infiltration and pleural effusion.
Inflammatory myofibroblastic tumor (IMT) is a distinctive lesion composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate usually composed of plasma cells and lymphocyte. ALK rearrangement is common in young adults but very uncommon in old adults. CT: IMT usually present as a peripheral well-circumscribed mass; irregular nodule or consolidation patterns are also reported. IMT shows variable FDG uptake. Histology: Microscopic examination shows spindle cells with minimal cytologic atypia admixed with inflammatory infiltrate composed of mainly lymphocytes and plasma cells (middle). ALK- IHC shows strong positivity, especially in the spindle cells (right).
Epithelioid hemangioendothelioma (EHE) is a low- to intermediate grade malignant vascular tumor seen most commonly in young female adults (60-80%). Lung involvement alone accounts for 12% and lung and liver involvement accounts for 18% of EHE.

CT: EHE presents in the thorax in following forms: 1) multiple nodular; 2) reticulonodular (interstitial); 3) diffuse pleural thickening (mimicking malignant mesothelioma); 4) peripheral mass with diffuse pleural thickening (mimicking lung cancer with pleural seeding).

Histology: It consists of polypoid or nodular aggregates of hyalinized eosinophilic stroma with a thin rim of plump endothelial cells.
CT: homogeneous contrast-enhancement, often pleural based without bone destruction, chest wall invasion or calcification.

Pathology: Synovial sarcoma is a soft tissue sarcoma with variable mesenchymal and epithelial differentiation. Biphasic pattern (small round cell and spindle cell) is present (middle). At least one epithelial marker and cytokeratin should be positive, with co-expression of vimentin or SMA. TLE-1 (upper right) is another specific marker for synovial sarcoma.
Pulmonary artery intimal sarcoma originates from the arterial intima of elastic pulmonary arteries.

**Imaging:** PA intimal sarcoma present as a **intraluminal mass with filling defects**. Extravascular extension into lung or mediastinum can be a diagnostic finding from pulmonary thromboembolism. PA intimal sarcoma may present as a large necrotic mass (arrow) mimicking NSCLC.

**Histology:** Gross and low-power specimen demonstrate large necrotic intraluminal mass.

*Arrow: intraluminal thrombus; Arrowheads: intraluminal mass.*
Pulmonary MALT lymphoma (extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue, BALT lymphoma) is thought to arise in acquired MALT secondary to inflammatory or autoimmune processes. **Imaging:** CT: 1) *single or multiple nodular or consolidative* (most common); 2) *bronchiectasis and bronchiolitis*; 3) *diffuse interstitial lung disease patterns*. FDG PET: variable FDG uptake

**Pathology:** MALY lymphoma generally appears as a diffuse infiltration of small lymphoid cells, which surround lymphoid follicles.
III. Lymphohistiocytic tumors

MALT lymphoma

MALT lymphoma: multi-nodular consolidation type

CT: Multiple ill-defined nodular lesions with ground-glass opacity and air-bronchogram (arrow).

Histology: Monotonous small lymphoid cells track along the bronchovascular bundles and interlobular septa at the periphery of the mass, with increased filling and destruction of alveolar parenchymal toward their center. Note the intact airway (arrow), which is correlated with air-bronchogram on CT.
Intravascular lymphomatosis is a rare aggressive extranodal diffuse large B-cell lymphoma, characterized by the presence of lymphoma cells within small vessels, particularly capillaries. Dyspnea and B symptoms are almost always present.

**Imaging:** Diffuse ground-glass opacity and centrilobular nodules are seen but CT may also be normal. Diffuse pulmonary FDG uptake on PET may be helpful if CT is normal.

**Pathology:** Lymphoma cells are identified within the lumens of small arteries, veins and capillaries (arrows), with no involvement of the alveolar spaces.
PLCH is caused by a proliferation of Langerhans cells with associated interstitial changes. Smoking is a strong risk factor (95%), and 15% of PLCH have extrapulmonary involvement. CT: irregular nodules with or without cavitation, evolving into cystic change with upper lung predilection. Pathology: Cellular proliferation of Langerhans cells along small airways. As the lesions enlarge, rounded nodules develop and bronchiolocentricity is not easy to discern. In end state, the nodules undergo a natural history progression from cellular lesions to fibrotic scars.
SUMMARY

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  - Radiologic-pathologic-genetic correlation helps to understand the pathophysiology of these rare lung tumors
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Thank you!

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