August 2014 Imaging Case of the Month

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Clinical History: A 42-year-old non-smoking woman presented with a history of relatively sudden onset left chest pain and shortness of breath. Her past medical history was remarkable for psoriasis, treated with Enbrel® (etanercept). She also had a history of partial hysterectomy for fibroids and right oophorectomy. Frontal and lateral chest radiography (Figure 1) were performed.

Figure 1. Frontal (A) and lateral (B) chest radiography.

Which of the following statements regarding the chest radiograph is **most accurate**?

1. The chest radiograph shows a left-sided pneumothorax
2. The chest radiograph shows a mediastinal mass
3. The chest radiograph shows bilateral linear and reticular opacities
4. The chest radiograph shows multifocal, bilateral consolidation
5. The chest radiograph shows numerous small nodules

Correct!

3. The chest radiograph shows bilateral linear and reticular opacities

The frontal chest radiograph shows curvilinear bilateral basal opacities and possible linear and reticular abnormalities, suggesting a possible interstitial infiltrative pulmonary abnormality, best seen in the right lung. These findings, while abnormal, are very non-specific. The abnormal findings at chest radiography are mostly linear and reticular in morphology; no small nodules are definitely seen. The lung volumes appear relatively normal. No pneumothorax is present. The heart is at most upper normal in size, but the mediastinal contours are otherwise normal. No areas of consolidation are present.

Which of the following represents the **next, most appropriate** step for the assessment of the findings at chest radiography?

1. ¹⁸FDG-PET scan
2. Fluoroscopic-guided percutaneous transthoracic needle biopsy
3. Thoracic CT
4. Thoracic MRI
5. Ventilation – perfusion scintigraphy

Correct!
3. Thoracic CT

Thoracic MRI can be employed for the investigation of mediastinal lesions, thoracic lymphadenopathy, chest wall lesions, and pleural abnormalities, but is less efficacious for the assessment of pulmonary abnormalities, particularly diffuse lung diseases; typically, thoracic CT is preferred for this application. Thoracic applications for ^{18}F FDG-PET scanning commonly include assessment of the solitary, indeterminate lung nodule and staging for pulmonary and extrathoracic malignancies; diffuse lung diseases are not typically evaluated with this modality. Some causes of alveolitis can produce elevated pulmonary parenchymal tracer uptake, as can pulmonary nodules in patients with sarcoidosis, but often these findings are incidentally detected at ^{18}F FDG-PET rather than intentionally evaluated with this technique. Ventilation-perfusion scintigraphy is commonly employed for the investigation of suspected pulmonary embolism, and less commonly to determine split lung function prior to pulmonary resections or to evaluate patients with pulmonary hypertension. In this circumstance, it would be reasonable to obtain ventilation-perfusion scintigraphy to assess for acute pulmonary embolism as a cause of the patient's complaints of chest pain and shortness of breath; however, ventilation-perfusion scintigraphy would not be useful for the evaluation of this patient's chest radiographic abnormalities. Transthoracic needle biopsy, either fluoroscopically or CT-guided, is primarily employed for establishing a diagnosis for focal pulmonary abnormalities, not diffuse lung disorders. Thoracic CT is the single best non-invasive test for characterizing the chest radiographic abnormalities).

Clinical course: The patient subsequently underwent unenhanced thoracic CT (Figure 2).

Figure 2: Axial unenhanced thoracic CT displayed in lung windows.

Which of the following statements regarding this imaging study is **most accurate**?

1. The thoracic CT shows a diffuse fibrotic process
2. The thoracic CT shows extensive centrilobular emphysema
3. The thoracic CT shows interstitial emphysema
4. The thoracic CT shows multiple, thin-walled pulmonary cysts
5. The thoracic CT shows numerous cavitory pulmonary nodules

Correct!

4. The thoracic CT shows multiple, thin-walled pulmonary cysts

The unenhanced thoracic CT shows multiple, bilateral, thin-walled cysts, without significant internal architecture, distributed fairly evenly throughout the upper, mid, and lower lungs. The cysts are slightly larger at the lung bases. No pulmonary nodules are present. The lesions present are best characterized as thin-walled cysts, rather than cavities or cavitory pulmonary nodules because of the lesions show very thin walls of uniform thickness with virtually no complexity. Typically, lesions that are referred to as “cavitory” are formed by tissue necrosis, and as a result, often have walls of varying thickness, internal architecture that may be nodular, and/or internal air-fluid levels; such features are lacking in this case. Centrilobular emphysema typically manifests at thoracic CT as small areas of circumscribed low attenuation *without* a definable wall, often showing a centrally positioned internal “dot” representing the centrilobular artery- this morphology is distinct from the morphology of the cystic lesions in this patient. Furthermore, centrilobular emphysema usually predominates in the upper lobes, whereas the cystic lesions in this patient are relatively evenly distributed in the upper, mid, and lower lungs. Finally, the patient was a non-smoker, further implicating a process other than centrilobular emphysema. Interstitial emphysema appears as linear areas of gas lucency tracking along the bronchovascular bundles, often associated with pneumomediastinum and subcutaneous emphysema, both of which are lacking in this patient. No features typical of fibrotic lung disease at CT- such as linear and reticular abnormalities, traction bronchiectasis, architectural distortion, and honeycombing- are not seen).

Which of the following assessments would be **suggestive of the correct diagnosis** in this patient, given the thoracic CT findings?

1. A careful examination of the skin
2. A detailed family history with genetic analysis
3. An autoimmune panel assessing for elevated inflammatory markers and antibodies, such C-reactive protein and the erythrocyte sedimentation rate, and SSA-, SS-B, anti-neutrophil cytoplasmic (ANCA), myeloperoxidase, complement titers, antinuclear antibody, anti-double –stranded DNA, and serine proteinase 3 autoantibodies
4. Review of prior abdominal imaging studies
5. All of the above

Correct!
5. All of the above

Choices 1,2,3 and 4 are correct, and therefore choice 5 is the best answer. The thoracic CT shows “cystic lung disease”- numerous thin-walled cysts relatively randomly distributed throughout the lung parenchyma. A careful analysis of the skin in this setting can be useful to assess for the presence of skin lesions- hamartomas of the hair follicles known as fibrofolliculomas- that may suggest the diagnosis of Birt-Hogg-Dubé syndrome. Similarly, a detailed family history and possibly a genetic analysis would be very useful as many patients with Birt-Hogg-Dubé syndrome and lymphangioleiomyomatosis have relatives with the disorders, as both conditions are associated with an autosomal dominant pattern of inheritance. The folliculin gene within chromosome band 17p111 is mutated in many patients with Birt-Hogg-Dubé syndrome, and therefore genetic testing can be of benefit for establishing this diagnosis. Patients with lymphangioleiomyomatosis frequently have mutations in the tuberous sclerosis genes TSC1 and TSC 2, whose protein products are hamartin and tuberin, respectively, and therefore genetic analysis is of benefit for establishing the diagnosis of lymphangioleiomyomatosis as well. Analysis of any prior imaging studies of the abdomen would be of benefit as patients with Birt-Hogg-Dubé syndrome frequently have hereditary renal tumors, such as chromophobe renal cell carcinomas and hybrid oncocytomas. Similarly, patients with lymphangioleiomyomatosis may have renal angiomyolipomas. Therefore, detection of solid renal lesions on abdominal imaging studies in patients with cystic lung disease specifically raises the possibility of either Birt-Hogg-Dubé syndrome or lymphangioleiomyomatosis. Finally, an “autoimmune panel”, including assessment of measures of systemic inflammation, such as C-reactive protein and the erythrocyte sedimentation rate, as well as various autoantibodies, such as SS-A, SS-B, anti-neutrophil cytoplasmic (ANCA), myeloperoxidase, complement titers, antinuclear antibody, anti-double –stranded DNA, and serine proteinase 3, would be useful to assess for autoimmune disorders that could be associated with lymphocytic interstitial pneumonia, which could potentially cause the cystic lesions in this patient).

Further clinical course. The patient underwent lip / minor salivary gland biopsy, which showed lymphocytic sialadenitis. Her erythrocyte sedimentation rate, C-reactive protein, PR-3 autoantibody and antinuclear antibody levels were all elevated. A polyclonal gammopathy was also noted. Flexible fiberoptic bronchoscopy showed no specific abnormalities (only non-specific chronic inflammation).

Which of the following would provide the **highest likelihood of establishing a diagnosis** for this patient?

1. ¹⁸FDG-PET scan
2. Catheter pulmonary angiography
3. Percutaneous transthoracic needle biopsy
4. Pleuroscopy
5. Video-assisted thoracoscopic lung biopsy

Correct!

5. Video-assisted thorascopic lung biopsy

Percutaneous transthoracic needle biopsy is typically employed for solid pulmonary, pleural, or chest wall targets; in the lungs, nodules are the typical target of this procedure. Cavities may be targeted in selected cases, but uniformly thin-walled cysts are not an appropriate target for this procedure. ¹⁸FDG-PET scan is a useful technique for the evaluation of focal pulmonary lesions and malignancy staging, and can be useful for selecting a target for tissue sampling when multiple indeterminate lesions are present, but would not provide management-altering information for this patient at this point of the patient's evaluation. Pleuroscopy can be useful for evaluating pleural space abnormalities, but such abnormalities are lacking in this patient. This patient's lesions reside within the lung, and therefore a lung-tissue sampling procedure is required. Catheter pulmonary angiography is useful for assessing right cardiac and pulmonary artery pressures as well as the pulmonary vasculature for thromboembolic disease, arteriovenous malformations, and / or vasculitis, but these disorders are not relevant considerations for this patient's cystic lung disorder. VATS has the ability to obtain enough pulmonary parenchymal tissue to allow a confident histopathologic diagnosis for the pulmonary abnormalities in this patient.

Further clinical course: The patient underwent video-assisted thorascopic (VATS) lung biopsy, which showed tissue characterized by large cystic spaces lined by moderately thickened fibrotic walls with chronic and follicular bronchiolitis, as well as mild patchy follicular interstitial hyperplasia, establishing the diagnosis of lymphocytic interstitial pneumonia. Given the patient's history of psoriasis treated with Enbrel (etanercept), the possibility of Enbrel (Etanercept)-induced Sjögren syndrome was entertained. This drug was discontinued and the patient was started on Imuran® (azathioprine) and prednisone to treat her combination of lymphocytic interstitial pneumonia and psoriatic arthritis. Her symptoms of shortness of breath and chest pain, as well as her psoriatic arthritis symptoms, greatly improved on therapy.

Diagnosis: Lymphocytic interstitial pneumonia

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