**RA DIOL OGY CA SE OF THE M ONTH**

**Pulmonary Langerhans Cell Histiocytosis**

Tatyana E. Fontenot, BA; Neal Viradia, MD; Elizabeth Pollard, MD; Harold Neitzschman, MD, FACR

*Purpose:* Obtaining a tissue sample diagnostic of pulmonary Langerhans cell histiocytosis (PLCH) by transbronchial biopsy is notoriously difficult. The condition’s appearance on computed tomography is well described and singularly characteristic, perhaps adequate for definitive diagnosis. We propose an approach to diagnosis of these patients.

*Methods:* Radiology case report of PLCH in a middle-aged female smoker with two week history of nonproductive cough, low grade fevers, and fatigue.

*Results:* Computed tomography (CT) provided the diagnosis of PLCH. Transbronchial biopsies failed to provide a definitive diagnosis.

*Conclusions:* Utility of transbronchial biopsy in diagnosis of PLCH is limited. Patients who present with signs, symptoms and high resolution computed tomography typical of PLCH do not require a correlation by tissue diagnosis. If cancer is suspected, a wedge biopsy should be performed for tissue diagnosis.

**CASE REPORT**

A 55-year-old woman presented with worsening nonproductive cough and shortness of breath. The cough had worsened over last two weeks despite use of over the counter cold medications. The patient experienced night sweats and weight loss over the last month. She had smoked a pack a day for the last 20 years.

**INTERPRETATION OF IMAGES**

The chest x-ray revealed reticular-nodular changes with bilateral areas of bronchiectasis and peribronchial thickening (Figure 1). A CT scan of the chest revealed upper and mid-lung fields full of small polymorphic cystic cavities, nodular opacities and bronchiectasis. Costophrenic angles were uninvolved. (Figure 2). CT axial slice at the level of the carina; (Figure 3). CT axial slice at the level of dome of the diaphragm; (Figure 4). CT reconstructed coronal slice.

The patient was diagnosed with PLCH based upon highly characteristic appearance on CT.

**DISCUSSION**

The title, Langerhans cell histiocytosis (LCH), describes syndromes that involve skin, bone, and viscera, the great majority of which present in pediatric populations. Pulmonary involvement in multisystem LCH portends an extremely poor outcome. However, isolated pulmonary Langerhans cell histiocytosis (PLCH) is a distinct entity that presents in a specific patient population and has good to fair prognosis depending on the stage at which it is diagnosed. This condition typically presents as shortness of breath with otherwise unimpressive physical findings in young adults with a history of smoking. Distinct and well described radiological features often provide the diagnosis.

Clinical features include nonproductive cough, fever, weight loss and malaise. More advanced disease can present with pulmonary hypertension, cor pulmonale, pulmonary function tests (PFTs) indicative of mixed obstructive, restrictive process and low carbon monoxide diffusing capacity (DLCO). A uniquely identifying clinical feature of this condition is the propensity of these patients for developing recurrent or bilateral pneumothoraces. Differential diagnoses include pneumatoceles and lymphangioleiomyomatosis.
Langerhans cells are dendritic antigen presenting cells with distinctive convoluted nuclear contour, presence of Birbeck granules on electron microscopy and positive staining with S-100 and CD1a. These bone marrow derived cells can be found throughout the normally functioning lung. PLCH is thought to be a reactive immune process due to tobacco smoke's antigenic properties. Tobacco glycoprotein stimulates production of tumor necrosing factor alpha (TNF-α), granulating macrophage colony-stimulating factor (GM-CSF), both of which recruit Langerhans cells and inhibit proliferation of lymphocytes which secrete interleukin-2 (IL2), an inhibitor of Langerhans cell recruitment and proliferation. Still, while numbers of these cells are elevated in majority of smokers, only a minority ever develop PLCH.

In the present case, tissue samples from two different transbronchial biopsies exhibited interstitial infiltration and diffuse fibrotic changes. While the samples contained cells that stained positively for S-100 and CD1a, these were sparse and deemed inadequate for diagnosis. This fact is unsurprising based upon similar previously described findings in late stage PLCH patients. Early in the disease course, the offending cells are abundant in proximal bronchial and bronchiolar epithelium. This pattern of distribution is consistent with histologic and radiologically evident features of the condition. As the disease progresses, the Langerhans cells recede from the end stage, fibrotic areas which then appear as hypocellular, stellate shaped scars and variable cysts in the pulmonary parenchyma that give rise to the
radiologic features (Figure 1). CT demonstrates nodules, reticular changes and in advanced disease, peribronchial irregularly shaped cysts of variable sizes in upper and middle lobes with characteristic sparing of the costophrenic angles. (Figure 1: Bottom left and bottom right). Presence of nodules on imaging has been found to be accurately predictive of an active disease process; however, a predominantly cystic appearance of lungs does not indicate cessation of disease activity.

LCH lesions of different ages are present throughout the course of the disease, however, it is the younger nodular lesions in periphery of the lung on CT images that are likely to harbor the exorbitant populations of Langerhans cells. Obtaining such a sample via bronchoscopy has been notoriously difficult. Video thoracoscopy and open biopsy have been successful methods of obtaining adequate samples for a confirmatory tissue diagnosis.

Treatment for PLCH is limited to smoking cessation and improvement of symptoms and spontaneous remission in patients who abstained is commonly reported. Still, in other cases, the disease progressed or rapidly entered end stage disease. Several studies report some benefit from treatment with steroids but this topic remains controversial. Lung transplantation is considered for patients with severe end stage disease; however the disease can recur in transplanted lungs. PLCH has also been associated with pulmonary malignancies, namely bronchogenic carcinoma that can arise pulmonary scar tissue.

Our patient’s evaluation was complicated by lack of congruity between characteristic radiologic imaging and the evaluation of limited transbronchial biopsy samples. Upon further review of diagnostic procedures and findings and extensive search of conditions with similar radiologic features, the original diagnosis was affirmed. Radiologic finding in our case overwhelmingly favored this singular diagnosis; more broadly we believe that it supports the preferential use of CT for definitive diagnosis and determination of prognosis of PLCH. Series reviews discuss a consistent difficulty in obtaining adequate tissue for diagnosis via transbronchial biopsy due to the patchy nature of the disease. We suggest that in the absence of physical examination, and laboratory findings suggestive of an alternate process, diagnosis made by CT does not require histological confirmation. This approach is appropriate due to the strength of radiological findings, indolent course of this condition and due to the limited nature of the treatment available. It spares the patient repeated needless invasive procedures. In cases where tissue diagnosis is imperative, either thorascopic or open biopsy should be the initial study offered to ensure selection of a diagnostically adequate sample. Such measures may be of most significant value in patients whose PLCH is suspected to coexist or given origins to pulmonary malignancies but are applicable in ruling out more aggressive interstitial lung disease.

REFERENCES


Tatyana Fontenu is a medical student at Tulane University School of Medicine. Dr. Viradia was a Tulane University Internal Medicine resident and is now a Radiology resident at New York University. Dr. Pollard is a chief resident at Tulane University Internal Medicine. Dr. Neitzschman, section editor, is a Professor of Radiology, and the Chairman of the Department of Radiology at Tulane UHSC.