CLINICAL VIGNETTE

Late Onset Isolated Pulmonary Langerhans Cell Histiocytosis

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Case Presentation

A 64-year-old male underwent a CT urogram for hematuria. Incidental findings included extensive groundglass opacities and centrilobular nodules of the lung. He denied chest pain, shortness of breath, fevers and chills, but he did report mild dyspnea on exertion. He had recently increased his exercise routine for weight loss purposes and initially thought dyspnea on exertion was secondary to deconditioning. His medical problems include hypertension, type 2 diabetes and paroxysmal atrial fibrillation. He smoked intermittently a half pack per day for 25 years. High resolution chest CT with contrast identified diffusely abnormal lung architecture with scattered interstitial reticulations, small nodules, and microcyst formations. Pulmonary function test showed no evidence of obstructive or restrictive ventilatory defect, but showed isolated reduction in diffusing capacity (55% predicted). He underwent left VATS procedure and lung wedge resection and lung biopsy which was positive for pulmonary Langerhans cell histiocytosis, confirmed by CD1a immunohistochemistry stain. Fungal and bacterial testing were negative. PET/CT showed no evidence of disease outside of the lung. Echocardiogram showed no evidence of pulmonary hypertension.

Discussion

Langerhans Cell Histiocytosis (LCH) is a rare disease that primarily affects children from one to three years old. However, the mean age at diagnosis for adults is age 35 with only 10% being > 55 years of age. Incidence is higher in Caucasians of northern European descent. There is no increased risk of LCH disease in family members. 45% of patients with LCH will have multisystem disease (mostly commonly bone and skin involvement).[1] Of the 55% with single organ system disease, only 10% of those patients will have isolated lung involvement whereas 70% of the single organ LCH will involve the bone. Isolated pulmonary Langerhans histiocytosis is also referred to as eosinophilic granuloma of the lung or pulmonary histiocytosis X and is considered a non-neoplastic process. There is no occupational or geographic predisposition, but nearly all affected individuals have a history of current or prior cigarette smoking. The prevalence of pulmonary LCH is likely underestimated as many patients are asymptomatic, they may have spontaneous remission prior to diagnosis, and radiographic findings may be nonspecific in the advanced form and, therefore, may not be specifically identified as PLCH.[2]

Clinical Presentation

Some patients with pulmonary LCH can go years without diagnosis, as they may have minimal to no symptoms. It is estimated that 20% of patients are diagnosed based on incidental imaging findings. Of the symptomatic patients, the most common symptoms are nonproductive cough, dyspnea, pleuritic chest pain, fatigue, we .ight loss and fever. Ten-20% of patients will present with spontaneous pneumothorax.[3] Because many pulmonary LCH patients have extensive smoking histories, the dyspnea and cough are attributed to smoking rather than LCH. Physical examination is often unremarkable. Routine laboratory studies are also unrevealing. Despite the name eosinophilic granuloma, the eosinophil count is normal in these patients. Pulmonary LCH patients are at a high risk for other thoracic complications including recurrent spontaneous pneumothorax (15-25% of patients), pulmonary hypertension, and hemoptysis. The development of pulmonary hypertension is associated with a poor prognosis with significant reduction in a patient's survival.[4]

Diagnostic Studies – The most sensitive diagnostic test is a high-resolution CT chest. Imaging will demonstrate interstitial fibrosis, multiple thick- and thin-walled cysts and cavitated nodules that frequently extend into the parenchyma of the lung surrounding the bronchovascular structures producing "stellate lesions" that are characteristic of the disease. Pulmonary LCH typically has a mid to upper lung predominance while sparing the costophrenic angles whereas idiopathic pulmonary fibrosis is predominantly in the lower lung zones.[5] Pulmonary function tests, including the total lung volume, may be completely normal. The most common functional abnormality (70-90%) is a disproportionally reduced diffusing capacity. As the disease progresses with more cystic components, airflow limitation and hyperinflation may develop. If the CT imaging is non-diagnostic, a combination of transbronchial lung biopsy and bronchoalveolar lavage (BAL) can be useful. Lung biopsies will demonstrate increased histiocyte markers CD1a, S100, and CD207 and will contain Birbeck granules (intracytoplasmic rod-shaped organelles with central striation). BAL is helpful for diagnosis when more than five percent of the BAL cells are CD1a positive and can help rule out infectious causes. BAL will often have a high macrophage count; however, it is considered a nonspecific finding as it reflects exposure to tobacco smoke.[6]

Treatment – Single system disease is rarely progressive and has a higher chance of spontaneous remission compared to multi-organ LCH. Most reports suggest five-year survival rates for

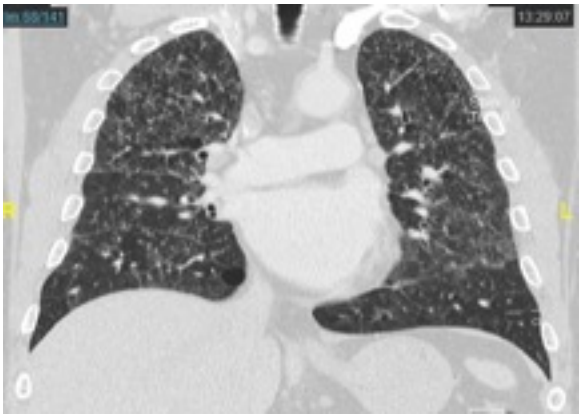
pulmonary LCH > 75%. Even with high survival rate, follow-up testing every three months in the first year after diagnosis may be helpful to identify patients more likely to have disease progression and relapse. Most patients with isolated pulmonary LCH require minimal to no treatment besides smoking cessation.[7] Oral corticosteroids and cytotoxic agents have not been helpful. Radiation therapy for bone lesions in multi-organ LCH patients can be helpful, but has no improvement in pulmonary LCH.[8] Case reports have shown that pulmonary hypertension associated with pulmonary LCH can be improved with advanced pulmonary hypertension therapies like sildenafil or bosentan.[9] However, in severe lung disease, lung transplant may be required. Unfortunately, recurrence of the condition in the transplanted lung may also occur.

Patient Outcome

Patient stopped smoking immediately after diagnosis. Repeat CT chest imaging 1 year after smoking cessation showed improved lung architecture with faded interstitial reticulations and ground glass attenuations. His dyspnea on exertion resolved.

Images

Image 1. High-resolution CT chest demonstrates diffuse interstitial reticulations, textured ground glass opacities with microcyst formation with upper lobe predominance and sparing of the posterior costophrenic angles.



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