CHEST

Smoking-Related Diffuse Cystic Lung Disease

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Exposure to cigarette smoke can lead to a variety of parenchymal lung diseases, including diffuse cystic lung diseases (DCLDs). Lymphangioleiomyomatosis (LAM) is the prototypical DCLD and has a characteristic appearance on high-resolution CT (HRCT). We present a series of four patients with DCLD on HRCT who were referred to our institution with a presumed diagnosis of LAM and who were found instead to have smoking-related injury of the small airways on histopathological analysis. We submit that cigarette smoke–induced small airway injury can present as DCLD on HRCT in a pattern that can mimic LAM. A detailed history of cigarette smoke exposure should be obtained in patients presenting with DCLD, and imaging features should not be used in isolation to establish a firm diagnosis of LAM.

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Exposure to cigarette smoke has been associated with a variety of diffuse parenchymal lung diseases, such as respiratory bronchiolitis-associated interstitial lung disease, desquamative interstitial pneumonia, pulmonary Langerhans cell histiocytosis (PLCH), acute eosinophilic pneumonia, and idiopathic pulmonary fibrosis.[1,2] Of these, PLCH most commonly manifests as a diffuse cystic lung disease (DCLD) on high-resolution CT (HRCT), and cystic changes have been reported in desquamative interstitial pneumonia.[3] The differential diagnosis of DCLDs is broad and, in addition to smoking-related diseases, includes diseases caused by a variety of pathophysiological mechanisms.[3,4]

ABBREVIATIONS: DCLD = diffuse cystic lung disease; HRCT = high-resolution CT; LAM = lymphangioleiomyomatosis; PLCH = pulmonary Langerhans cell histiocytosis

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Materials and Methods

We performed a retrospective chart review of four patients presenting to our institution with DCLD and a presumed diagnosis of lymphangioleiomyomatosis (LAM) who underwent surgical lung biopsy for diagnostic confirmation. Histopathological examination in all cases revealed changes consistent with smoking-related small airway damage including distal bronchioloectasis with mucostasis, emphysema, and cyst formation. Some of the results from this study have been previously reported in the form of an abstract.[5]

Results

All four patients were women with a mean age of 43.5 years (range, 31-53 years), which is a typical demographic in our LAM referral clinic. Dyspnea on exertion was the major presenting symptom in all four subjects, with two of the four also having chronic cough. None of the patients had a history of pneumothorax. Three of the four patients were active smokers with an average smoke exposure of 18 pack-years (range, 5-32), and one patient was largely homebound and had significant, near-constant secondhand exposure to cigarette smoke. Alpha-1 antitrypsin levels were normal in all patients. Other pertinent history and clinical findings included absence of sicca or serological findings to support the diagnosis of Sjögren syndrome, absence of skin lesions or family history of pneumothorax or renal neoplasms to support the diagnosis of Birt-Hogg-Dubé syndrome, and absence of tuberous sclerosis or renal angiomyolipomas to support the diagnosis of LAM. Serum vascular endothelial growth factor-D level was obtained on one patient and was nondiagnostic at 348 pg/mL. The remaining three patients were evaluated before the availability of serum vascular endothelial growth factor-D as a diagnostic biomarker for LAM.[6] A review of the HRCT images revealed the presence of multiple, round, thin-walled cysts of variable sizes distributed diffusely throughout the lung parenchyma. Some of the cysts were perivascular or contained internal structures, including septations or blood vessels (Fig 1). Centrilobular emphysema was present on HRCT in two of the four patients (Table 1, Fig 1).

All four patients had wedge biopsies from at least two lung lobes. Histopathologic analysis showed loss of alveolar density with multiple cystic spaces in all patients, corresponding to the diffuse cystic change seen radiographically (Fig 2). Alveolar walls of normal thickness surrounded and traversed the cystic spaces. Many of the cystic spaces were associated with small airways, with some of the spaces representing dilated distal bronchioles and alveolar ducts. Vessels were present in many of the walls of the cystic spaces,

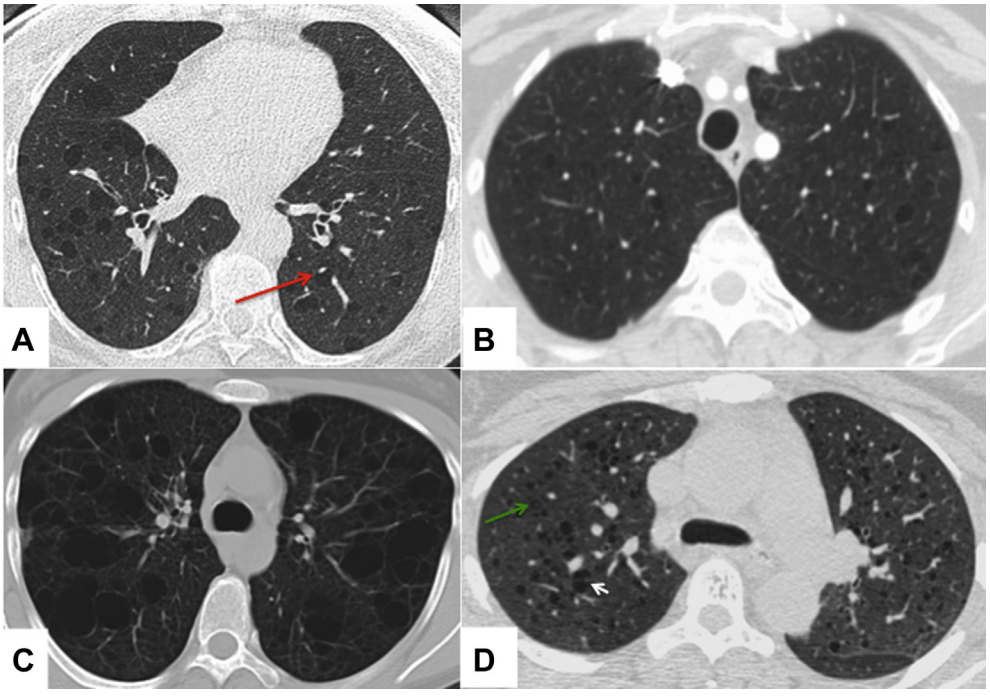

Figure 1 – *High-resolution chest CT scan images. A-D, Notice the presence of diffuse cystic change in all cases. Some of the cysts are perivascular (red arrow). Typical centrilobular emphysema is also seen in some instances (green arrow), as is thin internal septation (white arrow).*