Clinical-Radiologic-Pathologic Correlation of Smoking-Related Diffuse Parenchymal Lung Disease

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KEYWORDS

• Smoking • Fibrosis • Emphysema • Langerhans cell • Respiratory bronchiolitis • Desquamative interstitial pneumonia

KEY POINTS

- Cigarette smoking is considered the paradigm for chronic obstructive pulmonary disease because it causes injury, both permanent and reversible, to the large airways, small airways, and alveoli.
- Acute lung injury in the form of acute eosinophilic pneumonia can be seen in new-onset smokers, smokers who quit and restart smoking, and also the smokers who increase their daily use of cigarettes.
- The imaging and pathologic findings in pulmonary Langerhans cell histiocytosis evolve over time because the disease exists on a spectrum ranging from cellular to later fibrotic disease.
- Respiratory bronchiolitis and desquamative interstitial pneumonia represent a pathologic continuum, although the imaging findings can appear quite different.
- Fibrosis is a common finding in smoking-related lung disease and can range from mild alveolar wall fibrosis to diffuse nonspecific interstitial pneumonia and, in some cases, usual interstitial pneumonia.

INTRODUCTION

The smoke emerging from the mouthpiece of a cigarette is an aerosol containing about 10^{10} particles per milliliter.[1] This smoke is composed of more than 5000 types of chemicals, gases, and particulate matter that is both toxic and carcinogenic.[2] The direct toxicity of cigarette smoke and the body's subsequent response to this lung injury leads to a wide array of pathologic manifestations and disease states that lead to both reversible and irreversible injury to the large airways, small airways, alveolar walls, and alveolar spaces. This articles discusses these various forms of injury and how the pathologic manifestations lead to specific findings on computerized tomography (CT).

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Chronic obstructive pulmonary disease (COPD) represents a spectrum of disorders that lead to

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physiologic airflow limitation that is not entirely reversible.[3] Although there are various entities that can lead to COPD, cigarette smoking is considered the paradigm for this physiologic process because it causes injury, both permanent and reversible, to the large airways, small airways, and alveoli.[4] Because COPD is a physiologic abnormality, it should not be diagnosed on anatomic imaging. However, the underlying processes that lead to COPD in smokers, including large airways disease, small airways disease, and emphysema can be qualitatively and quantitatively assessed on imaging, most notably on CT.[5]

Inflammation of the large airways, or bronchitis, is a common clinical manifestation seen in patients who are smokers and is secondary to an innate immune response to the inhaled toxic particles and gases.[6] This immune response is mediated by various populations of T-cells, macrophages, and neutrophils that lead to the overproduction and hypersecretion of mucus from goblet cells in both the large and small airways.[7,8] In addition to the luminal narrowing from the mucus, the toxins also cause thickening, inflammation, and fibrosis of the bronchial and bronchiolar walls.[9] This leads to a further reduction in luminal diameter as well as a predisposition toward expiratory collapse of both the large and small airways.[8,10] All of these findings lead to dynamic airflow obstruction. On imaging, the walls of the large airways will be thickened and endobronchial mucus plugging may be visualized (**Figs. 1–3**).[11] Although there are numerous software programs that allow for the quantitative measurement of airway wall thickness using variable techniques, in most institutions this is a qualitative assessment and thus can be subjective.[12–15]

However, the injury to the airways goes beyond luminal narrowing. A study using pathologic findings and micro-CT correlation has shown a dramatic reduction in the number of small airways or obliteration or fibrosis of the lumen of small airways between 2 mm and 2.5 mm in diameter in smokers with even mild COPD compared with nonsmoking subjects.[10] In the lungs of subjects with centrilobular emphysema (CLE), there was, on average, a 99.7% reduction in the terminal bronchiolar cross-sectional area and an 89% reduction in the total number of terminal bronchioles per lung compared with nonsmoking control subjects. This injury leads to dilation and destruction of the centrilobular space, which surrounds the proximal respiratory bronchioles just downstream from the terminal bronchioles. It is this injury to the small airways, and not the emphysema itself, that is most responsible for the progression COPD.[16] Similar to bronchial wall thickening, the degree of small airways injury can be indirectly quantified through expiratory imaging, although this is beyond the scope of this article.[15,17]

Emphysema is the most common radiologic finding associated with cigarette smoking and is defined as the permanent enlargement of the airspaces distal to the terminal bronchioles. Various subtypes of emphysema exist but CLE is the most common subtype and has a well-proven association with cigarette smoking.[18,19] In CLE, more central alveoli adjacent to the small airways are dilated but the more peripheral alveoli adjacent to the septum that mark the boundary of the secondary pulmonary lobule are conspicuously spared (see **Fig. 2**). However, in severe disease, this classic pattern of CLE often becomes distorted because either the entire lobule appears to

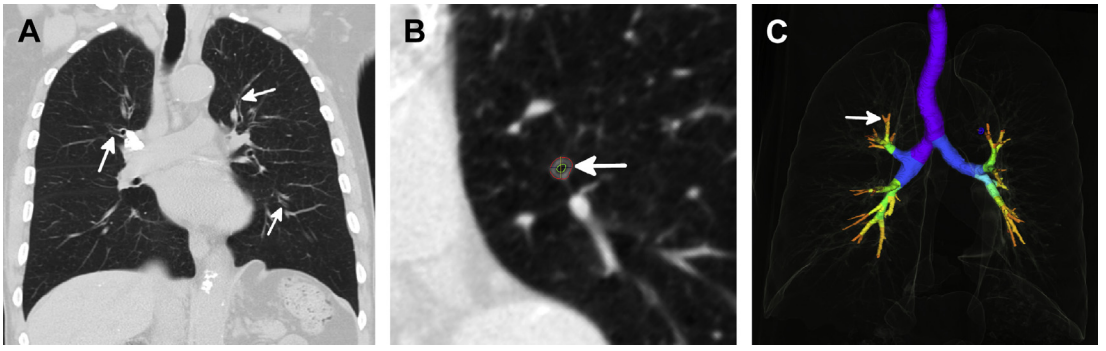

Fig. 1. Bronchial wall thickening due to cigarette smoking in an 80-year-old man. (*A*) Coronal image from a chest CT shows diffuse thickening of the bronchial walls (*arrows*). In most instances this is subjectively graded. (*B*) Coronal oblique image though a subsegmental bronchus in the anterior segment of the left upper lobe (*arrow*) demonstrates the ability of specialized computer software to analyze the bronchial lumen and wall thickness. (*C*) With these data, the software can generate a color-coded VRT map depicting various measurements including wall thickness. The airways coded yellow, orange, and red are more severely thickened (*arrow*).