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BRIEF REPORT

Pulmonary cysts in smoking-related interstitial fibrosis: a form of pseudocyst secondary to pulmonary interstitial emphysema

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KEYWORDS
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Abstract Smoking-related interstitial fibrosis is a distinct form of fibrosis, found in smokers, which has striking histopathological features. We present a case of pulmonary interstitial fibrosis with cysts in a 58-year-old woman who was a significant active smoker, presenting with a 7 month history of progressive dyspnea. TAC revealed thin-walled pulmonary cysts. An open lung biopsy was performed and the histopathological study showed hyaline fibrous thickening of the alveolar septa, respiratory bronchiolitis and cysts in the thickness of the interlobar septa. Immunohistochemically, the absence of an epithelial, vascular or lymphatic endothelial lining of the cysts would suggest that the cysts had been caused by pulmonary interstitial emphysema. Immunohistochemistry is essential in the differential diagnosis that includes, in this case, true cysts, pseudocysts and pulmonary lymphangiectasia.

PALABRAS CLAVE
Quistes pulmonares;
Fibrosis intersticial;
Tabaco;
Inmunohistoquímica;
Enfisema intersticial

Quistes pulmonares en el contexto de la fibrosis intersticial pulmonar relacionada con el tabaco: una forma de seudoquiste secundario a enfisema intersticial pulmonar

Resumen La fibrosis intersticial relacionada con el tabaco es una forma especial de fibrosis con histología característica que ocurre en fumadores. Presentamos un caso de fibrosis intersticial pulmonar con quistes en una mujer de 58 años con historia de tabaquismo importante, que refería disnea progresiva en los últimos 7 meses. La TAC reveló quistes pulmonares de

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paredes delgadas. Se realizó una biopsia pulmonar abierta y el estudio histopatológico mostró engrosamiento fibroso hialino de los septos alveolares, bronquiolitis respiratoria y quistes en el espesor de los septos interlobares. Inmunohistoquímicamente, la ausencia de revestimiento epitelial, endotelial vascular y linfático de los quistes, apoya que estos son causados por enfisema intersticial pulmonar. La inmunohistoquímica es esencial en el diagnóstico diferencial que incluye en este caso, quistes verdaderos, seudoquistes y linfangiectasia pulmonar.

Introduction

Smoking-related interstitial fibrosis (SRIF) is a distinct form of interstitial fibrosis with a striking pathological appearance that occurs in smokers. Clustered cysts with visible walls due to emphysema have been described.[1] We report a case of a patient with SRIF and septal pulmonary cysts caused by pulmonary interstitial emphysema (PIE).

Case report

A 58-year-old woman with a clinical history of significant active smoking (a pack a day for 40 years), presented with a 7 to 8 month history of progressive dyspnea. Lung function tests revealed a moderate mixed obstructive and restrictive process, with severe diffusion impairment, DLco (35% theoretical value) and 50% Kco (Krogh ratio). Arterial blood gases showed hypercapnic respiratory failure. A bilateral diffuse interstitial pattern with ground-glass areas and paraseptal emphysema was seen on high resolution computed tomography (HRCT) as were round, thin-walled cysts between the normal lung parenchyma (Fig. 1A). An open lung biopsy was performed; histopathology revealed hyalinised fibrosis thickening alveolar septa associated with emphysema in subpleural areas (Fig. 1B) and respiratory bronchiolitis (RB) (Fig. 1C). Oval, thin-walled cysts were present within the interlobar connective tissue septa (Fig. 1D) and the Masson trichrome staining showed pulmonary veins running through the septa (Fig. 2A). Immunohistochemistry with cytokeratin CAM 5.2 (CK) (Fig. 2B), CD34, CD31 (Fig. 2C) and D2-40 (Fig. 2D) showed absence of epithelial, vascular or lymphatic endothelial lining in the cysts.

Discussion

Cigarette smoking can cause a variety of diffuse lung diseases, with a typical cystic pattern in the case of pulmonary Langerhans cell histiocytosis (PLCH), and ground glass pattern often with cysts in patients with respiratory bronchiolitis associated interstitial lung disease (RBILD) and SRIF.

In RBILD and SRIF the cysts are located in the lower lung and subpleural regions, whereas in PLCH the nodular pattern and multiple bizarre-shaped cysts occur predominantly in the upper and middle lung zones.

Histologically, these cysts are emphysematous spaces of irregular morphology delimited by walls thickened by fibrosis. Other cystic lesions have been described as airspace enlargement with fibrosis (AEF). The wall thickness of this cystic lesion (0.8 mm) is thinner than that found in interstitial pneumonia (UIP) (2.1 mm) and thicker than in emphysema (0.07 mm).[2] This cystic lesion described as AEF, although not well defined, frequently accompanies centrilobular emphysema and may represent emphysema with fibrous walls.

The term SRIF was first used by Katzenstein [3] to describe a distinctive form of severe interstitial fibrosis with accompanying respiratory bronchiolitis and emphysema. We describe, in a patient with SRIF, diffuse pulmonary cysts of septal location and without lining of any type, suggesting that cysts are caused by PIE. PIE typically occurs in the respiratory distress syndrome or bronchopulmonary dysplasia, although it has also been described in UIP.[4] However, cysts caused by PIE have not been described associated with SRIF. PIE is an acquired condition in which air enters into the interstitial tissue as a consequence of barotrauma, dissecting bronchovascular structures and connective tissue septa. In our patient, the absence of barotrauma suggests that cigarette smoke-induced matrix degradation, in distal lung tissue as described in RBILD, SRIF and PLCH cysts,[5] could be the pathogenic mechanism involved in the interstitial emphysema and formation of these pulmonary cysts.

On chest radiographs a cyst is defined as a thin-walled (< 2 mm), spherical parenchymal lucency interfaced with normal lung. However, microscopically, a cyst is characterized by the lining epithelium the nature of which can be identified using immunohistochemistry. We propose that cysts due to PIE are denominated aerial pseudocysts because they lack epithelial and endothelial lining.

The differential diagnosis should include true cysts, cyst-like spaces and diffuse pulmonary lymphangiectasia (DPL) (Table 1). True cyst lining shows ciliated epithelium expressing CKs. This is what happens in pulmonary cystic adenomatoid malformation, in bronchiolectasis and respiratory-lined cysts. The latter show a positive correlation with honeycombing but differ because only the bronchiolectasis have a uniform muscle layer in the wall.[4] A cyst-like space is characterized by a discontinuous epithelial lining as a result of loss of lung parenchyma, as seen in emphysema, post-traumatic cyst, some infections, sarcoidosis, Birt-Hogg-Dubé syndrome (BHD),[6] RBILD,

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