

Airway-Centered Interstitial Fibrosis Associated With Exposure to Fumes From Cleaning Products

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Airway-centered interstitial fibrosis is a little known clinical entity that has only recently been described in the literature. Its pathology is characterized by bronchial fibrosis and localized interstitial pulmonary fibrosis around the airways. The disease has been associated with inhalation of a variety of substances, environmental or occupational, organic or inorganic. Clinical signs, radiographic manifestations, and lung function in patients with airway-centered interstitial fibrosis are similar to those of patients with idiopathic interstitial pneumonia.

We describe a case of airway-centered interstitial fibrosis related to exposure to fumes from cleaning products.

Key words: Diffuse interstitial pulmonary disease. Idiopathic interstitial pneumonia. Airway-centered interstitial fibrosis.

Fibrosis pulmonar intersticial centrada en las vías aéreas asociada a inhalación de productos de limpieza

La fibrosis pulmonar intersticial centrada en las vías aéreas es una entidad clinicopatológica poco conocida y de reciente descripción, que se caracteriza anatomopatológicamente por fibrosis bronquiolar y fibrosis pulmonar intersticial localizada alrededor de las vías aéreas. Esta enfermedad se ha relacionado con la inhalación de diversos agentes tanto ambientales como ocupacionales, de origen orgánico o inorgánico. Las manifestaciones clínicas, radiológicas y funcionales respiratorias son similares a las de las neumonías intersticiales idiopáticas.

Se describe un caso de fibrosis pulmonar intersticial centrada en las vías aéreas que fue secundaria a la inhalación de productos de limpieza.

Palabras clave: Enfermedades pulmonares intersticiales difusas. Neumonías intersticiales idiopáticas. Fibrosis pulmonar intersticial centrada en las vías aéreas.

Introduction

In 2002 the American Thoracic Society and the European Respiratory Society drafted a consensus statement classifying the diverse idiopathic interstitial pneumonias.¹ In all such pneumonias, pathological diagnosis relies on the presence of inflammatory and fibrotic lesions that affect the pulmonary parenchyma diffusely.² However, few diffuse interstitial lung diseases are characterized by histological abnormalities in the alveoli and terminal bronchioles. Of these few, the most common and well defined are hypersensitivity pneumonitis and respiratory bronchiolitis associated with interstitial lung disease.^{3,4} Recently there have been reports of new clinicopathologic entities with

radiographic manifestations and repercussions on lung function that are characteristic of interstitial idiopathic pneumonias but with such pathologic abnormalities as bronchiolar fibrosis and interstitial fibrosis surrounding the airways.⁵⁻⁷

Of these conditions, the most well-defined is airway-centered interstitial fibrosis,⁵ a rare entity that has only recently been described and is associated with the inhalation of diverse agents—environmental and occupational, organic and inorganic. In the present report we describe a case of airway-centered interstitial fibrosis related to inhalation of fumes from cleaning products.

Case Description

The patient was a 51-year-old woman, ex-smoker of 10 pack years, with a history of lumbar scoliosis, recurrent bouts of renal colic, and acute hepatitis. The most noteworthy occupational risk factor prior to diagnosis of lung disease was a 4-year period when, as a cleaning service employee, she

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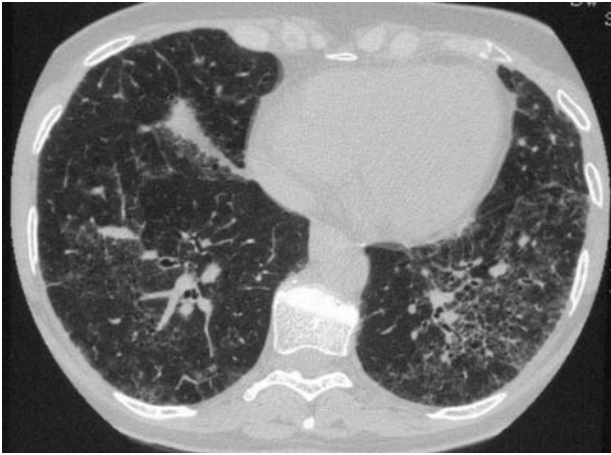


Figure 1. High resolution computed tomography scan of the chest showing thickening of the bronchiolar walls, peribronchovascular reticulation, and ground glass opacities.

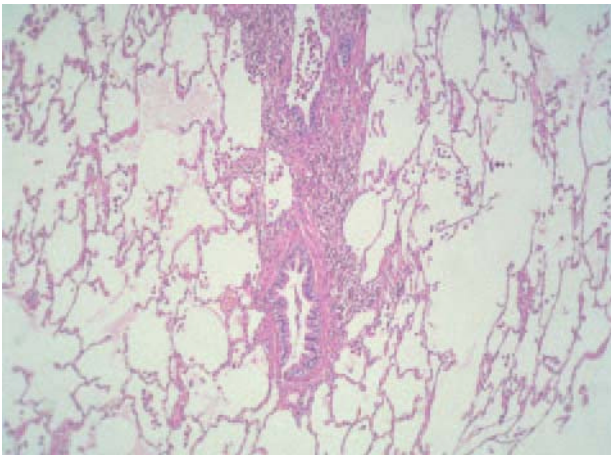


Figure 2. Lung biopsy: peribronchiolar fibrosis. (Masson-trichrome stain, original magnification $\times 400$).

washed floors in poorly ventilated areas using a solution of 25% hydrochloric acid, 55% sodium hydroxide (pH, 14), surfactants, and glycols. During the time of exposure she had a dry cough and experienced dyspnea with moderate exercise. One year prior to diagnosis she developed fever and alveolar infiltrates in the left lower lobe—a clinical picture diagnosed as community-acquired pneumonia. The symptoms resolved with antibiotic treatment.

The patient came to our department complaining of persistent cough and progressive dyspnea. Physical examination revealed clubbing in both hands. Auscultation detected no rales. Nor were abnormalities detected in blood test results. A chest radiograph showed a bilateral reticulonodular interstitial pattern, mainly in the inferior lobes. Lung function testing revealed a restrictive ventilatory defect of moderate intensity: a forced vital capacity (FVC) of 2.05 L (69% of predicted), forced expiratory volume in the first second (FEV₁) of 1.77 L (75% of predicted), and a FEV₁/FVC ratio of 86.08. The testing also revealed a reduction in lung volumes (a total lung capacity of 3.60 L, 74% of predicted) and a marked reduction in carbon monoxide diffusing capacity (10.39 mL/min/mm Hg, 47% of

predicted). Blood gas findings were normal. High resolution computed tomography showed thickening of the bronchiolar walls, peribronchovascular reticulation, bronchiolectasis, patchy areas of ground glass opacities, and slight honeycombing (Figure 1). Fiberoptic bronchoscopy showed no macroscopic abnormalities in the tracheobronchial tree. Results of bronchoalveolar lavage cytology were normal. A transbronchial biopsy was performed, but the specimens were inadequate for study of the interstitial lung abnormalities. Video-assisted thoracoscopic lung biopsy revealed a predominance of bronchiolar lesions, fibrotic thickening of peripheral airway walls, and an accumulation of mixed-dust-laden macrophage cells whose polarization showed no noteworthy birefringent elements. No granulomatous structures were observed. The dense hyalinized fibrosis of the airways hardly extended farther than the contiguous alveoli. The lung parenchyma showed signs of only centrilobar emphysema with fibrotic thickening of the bronchiolar walls. Histological abnormalities supported the diagnosis of airway-centered interstitial fibrosis (Figure 2).

A regimen of prednisone was initiated with high doses, which were gradually reduced to a maintenance dose of 10 mg/d. A dose of 150 mg/d of azathioprine was subsequently added. Despite treatment, lung function showed progressive decline in FVC and carbon monoxide diffusing capacity.

Discussion

In 2002 the American Thoracic Society and the European Respiratory Society drafted a consensus statement on the classification of idiopathic interstitial pneumonias.¹ Since publication of the statement, 3 clinicopathologic entities with radiologic manifestations and characteristic respiratory function findings have been identified as belonging to this category of pneumonia. The pathologic abnormalities characteristic of the 3 conditions fall under the subcategory of bronchiolocentric fibrosis and they can be distinguished from the abnormalities of the diseases included in the consensus statement. The 3 entities have been named centrilobular fibrosis, airway-centered interstitial fibrosis, and idiopathic bronchiolocentric interstitial pneumonia.⁵⁻⁷

Churg et al⁵ recently reported 12 cases of a clinicopathologic condition named airway-centered interstitial fibrosis. The authors associated the disease with inhalation of diverse agents—environmental or occupational, organic or inorganic—because 8 of the patients had a history of exposure to birds or to other potentially toxic substances: wood smoke, chalk dust, cotton fibers, dust from fodder, agricultural chemical compounds, and cocaine. Findings on computed tomography chest scans are not well defined, although reticulation indicative of peribronchovascular fibrosis and traction bronchiectasis are present in most cases and honeycombing is sometimes observed. Histologic lesions are characterized by bronchiolar fibrosis and bronchiolocentric interstitial fibrosis surrounding the bronchioles and possibly the central airways.⁸ The disease, which has a poor prognosis, does not usually respond to glucocorticoid treatment regimens. The case we report presented the clinical, radiologic, and

pathologic signs of airway-centered interstitial fibrosis. The patient was a woman whose exposure to fumes from cleaning products had a close relation to the onset of symptoms; this supports the hypothesis that airway-centered interstitial fibrosis may be caused by inhalation of toxic substances. In our patient, as in those described by Churg et al,⁵ the course of disease was unfavorable and there was no response to glucocorticoids and immunodepressants.

Besides airway-centered interstitial fibrosis, reports of 2 other conditions with similar clinicopathologic characteristics have appeared in the literature. Yousem and Dacic⁶ reported 10 cases of an entity named idiopathic bronchiolocentric interstitial pneumonia, characterized by centrilobular inflammation and fibrosis of the small airways with limited peribronchiolar interstitial involvement. The only difference between this entity and airway-centered interstitial pulmonary fibrosis is that idiopathic bronchiolocentric interstitial pneumonia also affects the small bronchioles. The etiology of idiopathic bronchiolocentric interstitial pneumonia is unknown, although it may be a form of hypersensitivity pneumonitis. No clinical evidence of hypersensitivity pneumonitis was detected in the cases reported, however, although it is possible that the causal agent went undetected. As with airway-centered interstitial pulmonary fibrosis, idiopathic bronchiolocentric interstitial pneumonia is progressive and the prognosis poor.⁶ De Carvalho et al⁷ reported 12 cases of another clinicopathologic condition: centrilobular fibrosis. This entity is characterized by fibrosis of the centrilobular areas and necrosis of the bronchiolar epithelium, but without the extension observed in airway-centered interstitial fibrosis. The authors considered centrilobular fibrosis to be related to the aspiration of gastric content. Gastroesophageal reflux can be an etiological factor in idiopathic pulmonary fibrosis, and pathologic lesions of centrilobular fibrosis have been observed in animal models of aspiration and in patients with aspiration pneumonias.^{9,10} However, the existence of gastroesophageal reflux was not clearly specified in the cases reported. Prognosis is unknown, as de Carvalho et al included no information on the course of disease in their patients.

It is yet to be determined whether these conditions characterized by peribronchiolar fibrosis are well-differentiated diseases, pulmonary fibrotic responses secondary to various etiologies, or different stages of the same disease. At any rate, these entities involve clinical signs characteristic of diffuse interstitial diseases, but their histologic lesions are limited to bronchiolar zones. Their inclusion as well-differentiated pathologic entities in the classification of diffuse interstitial pulmonary diseases is yet to be determined.

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