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Case Report

Diffuse Interstitial Lung Disease Related to Peribronchiolar Metaplasia

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ABSTRACT

Peribronchiolar metaplasia is a histologic lesion characterized by fibrosis and bronchiolar epithelial proliferation, affecting peribronchiolar alveolar septa and terminal bronchioles. It has been considered a nonspecific tissue reaction secondary to the action of external factors, such as tobacco smoke and microbes, and is a common histologic finding in several diffuse interstitial lung diseases. Several such cases with clinical, radiologic, and lung function manifestations characteristic of idiopathic interstitial pneumonia have been described recently, all having peribronchiolar metaplasia as the only histologic abnormality. We report 2 cases of interstitial lung disease in which peribronchiolar metaplasia was the only finding of pathology.

Enfermedad pulmonar intersticial difusa por metaplasia peribronquiolar

Palabras clave:
Enfermedades pulmonares intersticiales difusas
Neumonías intersticiales idiopáticas
Metaplasia peribronquiolar

RESUMEN

La metaplasia peribronquiolar es una lesión histológica caracterizada por fibrosis y proliferación del epitelio bronquiolar, que afecta a las paredes alveolares peribronquiales y a los bronquíolos terminales. Se considera una reacción tisular inespecífica secundaria a la acción de factores externos, tales como el humo del tabaco y agentes microbianos. Es un hallazgo histológico frecuente en diversas enfermedades pulmonares intersticiales difusas. Recientemente se han descrito algunos casos de enfermedad pulmonar intersticial difusa con manifestaciones clínicas, radiológicas y de función respiratoria propias de las neumonías intersticiales idiopáticas en que la única alteración histológica era la presencia de metaplasia peribronquial. En el presente artículo se describen 2 casos de neumopatía intersticial donde el único hallazgo anatomopatológico era la metaplasia peribronquiolar.

Introduction

Peribronchiolar metaplasia is a histologic lesion characterized by fibrosis and bronchiolar epithelial proliferation in the peribronchiolar alveolar septa, extending to the terminal bronchioles through the canals of Lambert. It has been reported as a nonspecific tissue reaction secondary to the action of external factors, such as tobacco smoke and microbes.[1] In this context, peribronchiolar metaplasia has been observed in adenovirus and mycobacterial infections, as well as in patients with lung cancer.[1] It is also a common but chance finding of uncertain significance in various diffuse interstitial lung diseases.[2] Several recently described cases of diffuse interstitial lung disease gave peribronchiolar metaplasia as the only histologic change.[2] We describe 2 cases of interstitial lung disease in which peribronchiolar metaplasia was the only finding of pathology.

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Case Descriptions

Patient 1

The patient was a 53-year-old woman who was an ex-smoker of 30 pack-years with no known history of occupational exposure of interest. Relevant aspects of her medical history included an episode of deep vein thrombosis in the right lower limb and fibromyalgia, which was being treated with oral analgesics. Dyspnea on exertion started 5 years previously and had progressed, but there were no other associated symptoms. The physical examination revealed a pleural rub and inspiratory rales predominantly in the left base. Bilateral malleolar edema was also present, mainly in the evening. A chest radiograph showed pleural calcifications with no other abnormalities. Lung function assessment revealed diminished carbon monoxide diffusing capacity (16.41 mL/min/mm Hg; 71% of reference). A ventilation-perfusion lung scan was normal and the immunological study was negative. A stress test on a cycle ergometer revealed moderately reduced exercise tolerance, with normal ventilatory and cardiac reserves, and a slight increase in the alveolar-arterial oxygen gradient. A high-resolution computed tomography (CT) scan of the chest revealed subpleural fibrotic bands, septal thickening mainly at the base of the left lung, and centrilobular nodules of ground-glass opacity in the upper lobes, indicative of respiratory bronchiolitis-associated interstitial lung disease or hypersensitivity pneumonitis. An echocardiogram was normal. Diffuse interstitial lung disease was suspected and fiberoptic bronchoscopy was performed but showed no macroscopically evident lesions. Microbiology and cytology of the bronchial aspirate were negative and cellular analysis of the bronchoalveolar lavage fluid was normal. A lung biopsy was taken by video-assisted thoracoscopy. Histology suggested peribronchiolar metaplasia, given bronchioles with reactive changes in the form of tunneling through the epithelium to adjacent ducts and slight septal fibrosis. These findings were not associated with significant inflammatory changes or distal abnormalities.

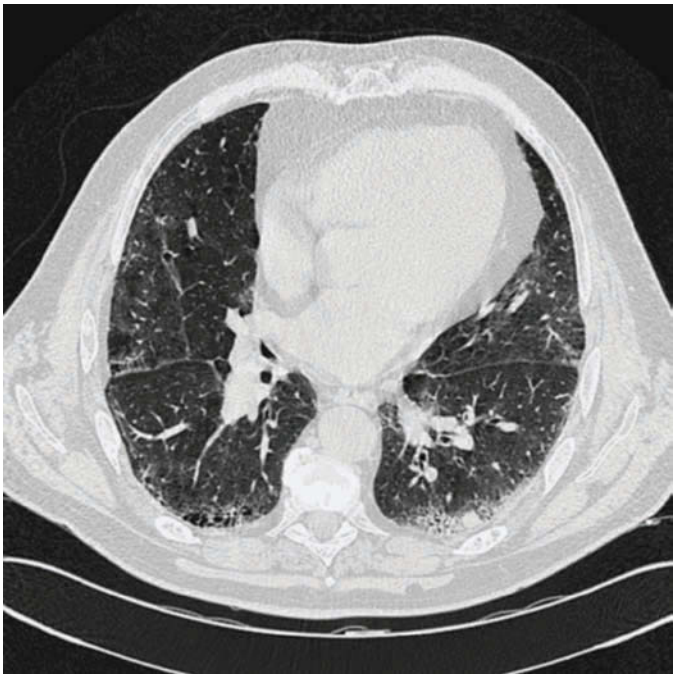

Figure 1. Computed tomography scan showing areas of ground-glass attenuation and small subpleural cystic images in the base of the right lower lobe, for a differential diagnosis of either emphysema or honeycombing.

Patient 2

The patient was a 58-year-old man with a history of hypertension and poor venous return. He was an ex-smoker of 60 pack-years with no known occupational history of interest. He also had a 9-year history of productive cough, dyspnea on exertion, and episodes of bronchospasm. Pulmonary emphysema was revealed by high-resolution CT of the chest. A follow-up CT scan showed signs of biapical emphysema and subpleural patches of ground-glass opacity in both lung bases, indicating usual interstitial pneumonia or nonspecific interstitial pneumonia (Figure 1). The physical examination and blood test results were normal. Lung function assessment revealed mild obstructive ventilatory defects: a ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) of 73%, FEV_1 of 2.8 L (79% of reference), FVC of 3.85 L (82%), a negative bronchodilator test, a decrease in total lung capacity (5.1 L, 71%), and a marked reduction in carbon monoxide diffusing capacity (13.4 mL/min/mm Hg, 45% of reference values). Fiberoptic bronchoscopy showed diffuse inflammation of the bronchial mucosa. Bronchoalveolar lavage fluid cell counts were normal. A lung biopsy was taken by video-assisted thoracoscopy. Histology indicated peribronchiolar metaplasia, given metaplastic extension of the bronchiolar epithelium towards the alveolar ducts and adjacent alveoli, with focal chronic inflammation and slight fibrosis of the lamina propria (Figure 2). Treatment was initiated with bronchodilator medication and inhaled corticosteroids. There were no clinical or lung function changes after 1 year.

Discussion

Peribronchiolar metaplasia consists of bronchiolar epithelial proliferation and fibrosis of the peribronchial alveolar septa, extending to the bronchiolar mucosa through the canals of Lambert. It is a histologic finding of uncertain significance, sometimes considered a reaction of the tissue to the action of various external factors, such as infections and tobacco smoke; alternatively, it might be an epiphenomenon in bronchopulmonary tumors.[1] It is also a common finding in diffuse interstitial lung diseases. Fukuoka et al[2] reviewed the histologic changes in 106 cases of interstitial lung diseases, observing that peribronchiolar metaplasia was present in 59% of usual interstitial pneumonias, in 50% of nonspecific interstitial pneumonias, in 50% of desquamative interstitial pneumonias, in 50%

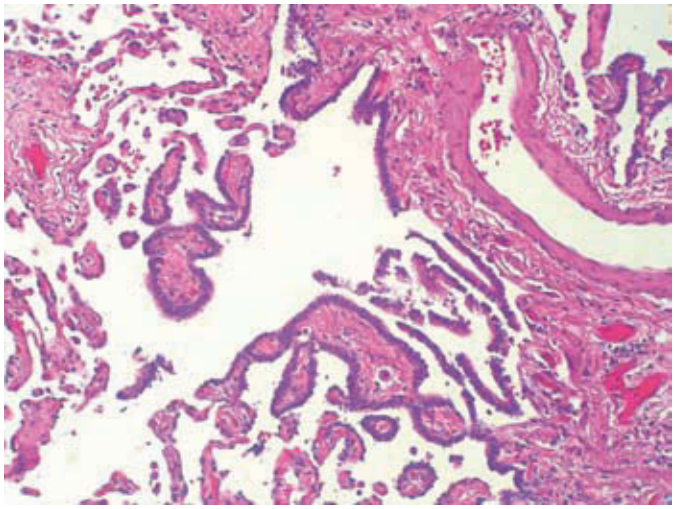

Figure 2. Microscopic image of the lung parenchyma showing a bronchiole whose epithelium extends to adjacent alveolar ducts accompanied by slight fibrosis. (Hematoxylin-eosin, ×100.)

of cases of hypersensitivity pneumonitis, and in 11% of cases of respiratory bronchiolitis-associated interstitial lung disease.

Fifteen cases of diffuse interstitial lung disease described recently gave peribronchiolar metaplasia as the only histologic finding.[2,4] The clinical picture in those cases included the clinical, radiologic, and lung function manifestations typical of idiopathic interstitial pneumonia. The etiology of this clinicopathologic entity has not been determined, although 3 of the patients described had collagen diseases (mixed connective tissue disease, rheumatoid arthritis), and another was positive for antinuclear antibodies with no associated rheumatic symptoms. One patient was a welder with a history of exposure to asbestos, and another had been regularly exposed to pigeons; 54% of patients were smokers. High resolution CT findings varied considerably, although the most common image was mosaic attenuation during expiration.[2] The prognosis seems to be good, since a follow-up of 11 of the 15 patients for over 2 years showed the disease to be stable.

We have described 2 cases of diffuse interstitial lung disease in which peribronchiolar metaplasia was the only histologic finding. Our patients were middle-aged and presented with progressive dyspnea. The CT signs indicated diffuse interstitial disease, suggesting a diagnosis of hypersensitivity pneumonitis or respiratory bronchiolitis in the first case, and usual interstitial pneumonia or nonspecific interstitial pneumonia in the second. Both patients were ex-smokers, with no known occupational history of interest or exposure to substances that cause hypersensitivity pneumonitis, and they did not present signs, symptoms, or biological abnormalities associated with collagen diseases.

Since the 2002 consensus statement of the American Thoracic Society and European Respiratory Society, besides interstitial lung disease related to bronchiolar metaplasia, additional clinicopathologic entities characterized by bronchiolar disease with or without peribronchial fibrosis have been described in association with clinical, radiologic, and lung function manifestations characteristic of idiopathic interstitial pneumonia.[5-8] Interstitial pulmonary fibrosis of the airways is a clinicopathologic entity with a poor prognosis, associated in most cases with a history of exposure to environmental, occupational, and organic and inorganic substances such as bird droppings, wood smoke, cocaine, chalk dust, cotton fibers, and cleaning products.[5,9] De Carvalho et al[7] have also described another entity known as centrilobular fibrosis with pathologic findings similar to those caused by gastric content aspiration. However, their patients had no histories of gastroesophageal reflux disease. Idiopathic bronchiolocentric interstitial pneumonia is another entity with histologic characteristics similar to those of hypersensitivity pneumonitis, except for the absence of interstitial granulomas. However, the cases described had no background of exposure to organic and inorganic substances.[6,10]

It is notable that in all 3 of these clinicopathologic entities, foci of bronchiolar metaplasia were observed in some patients. It is also possible that these entities, together with bronchiolar metaplasia related to interstitial lung disease, may be different stages of the same disease but limited to the bronchiolar zones. However, the likelihood of their being distinct clinical entities cannot be ruled out. Their inclusion as such in the classification of diffuse interstitial lung diseases is yet to be determined.

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