CHEST

Airway-Centered Fibroelastosis
A Distinct Entity

Pauline Pradere, MD; Clément Gauvain, MD; Claire Danel, MD; Marie Pierre Debray, MD; Raphael Borie, MD; Laurent Plantier, MD, PhD; Hervé Mal, MD; Michel Aubier, MD, PhD; Bruno Crestani, MD, PhD; and Camille Taillé, MD, PhD

OBJECTIVE: To describe a new entity characterized by airway-centered fibroelastosis.

METHODS: We identified cases with prominent airway-centered elastosis in lung samples, and little or no pleural involvement identified through a pathologic database at a single institution over an 8-year period.

RESULTS: Airway-centered fibroelastosis was characterized by (1) extensive airway-centered fibroelastosis of the upper lobes on histopathology and (2) marked bronchial abnormalities with bronchial wall thickening, bronchial wall deformation, and bronchiectasis, along with progressive parenchymal retraction and predominantly subpleural upper-lobe consolidations on high-resolution CT. Pateints were five nonsmoking women aged between 38 and 56 years old. They experienced chronic dyspnea with acute attacks of wheezing and dyspnea. Moderate to severe physiological abnormalities were observed, with an obstructive pattern in three cases and a restriction in two. Despite inhaled and oral corticosteroids, the disease was progressive in all patients and evolved to chronic respiratory failure, requiring lung transplantation in two patients. Four patients had chronic asthma.

CONCLUSIONS: We consider airway-centered fibroelastosis to be a unique and distinct pathological entity in women that needs to be individualized, with a specific clinical, imaging, and pathological presentation. We hypothesize that airway-centered fibroelastosis may be idiopathic or asthma-associated. CHEST 2016; 149(3):767-774

KEY WORDS: asthma; chronic obstructive pulmonary disease; idiopathic disease; interstitial lung disease

ABBREVIATIONS: ABPA = allergic broncho-pulmonary aspergillosis; HOB = hypereosinophilic obliterative bronchiolitis; HRCT = high-resolution CT; PPFE = pleuropulmonary fibroelastosis

AFFILIATIONS: From the INSERM U1152 (Drs Pradere, Gauvain, Danel, Borie, Plantier, Mal, Aubier, Crestani, and Taillé), Paris, France; University Paris Diderot (Drs Pradere, Gauvain, Danel, Borie, Plantier, Mal, Aubier, Crestani, and Taillé), Sorbonne Paris Cité, Paris, France; Service de Pneumologie A (Drs Pradere, Gauvain, Borie, Aubier, Crestani, and Taillé), Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Département hospitalo-universitaire FIRE, Competence Center for Rare Pulmonary Diseases, Paris, France; Département d'Anatomie Pathologique (Dr Danel), Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France; Service de Radiologie (Dr Debray), Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France; Service d'explorations fonctionnelles (Dr Plantier), Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France; Service de Pneumologie et Transplantation (Dr Mal), Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France.

Drs Crestani and Taillé contributed equally to this manuscript.

CORRESPONDENCE TO: Bruno Crestani, MD, PhD, Hôpital Bichat, Service de Pneumologie A, 46 rue Henri Huchard, 75018 Paris, France; e-mail: bruno.crestani@bch.aphp.fr

DOI: http://dx.doi.org/10.1016/j.chest.2015.10.065

Remodeling of the airways is well-described in chronic asthma and was first described in autopsy studies of individuals dying of asthma. These studies demonstrated changes in large and small airways including mucus plugging, epithelial detachment, goblet cell metaplasia, basement membrane thickening, subepithelial fibrosis, and smooth muscle and mucous gland hypertrophy.[1]

Remodeling of bronchial elastin fibers has been occasionally reported in patients with asthma.[2-6] We report a group of patients with longstanding chronic asthma and a unique remodeling pattern characterized by an extensive airway-centered fibroelastosis leading to chronic respiratory insufficiency and eventually requiring lung transplantation.

Materials and Methods

Case Descriptions

We identified five patients with histological evidence of prominent airway-centered elastosis in lung samples, and little or no pleural involvement. The cases were identified through a pathologic database at a single institution over an 8-year period (2006-2014). Over the same period, 126 surgical lung biopsies and 228 lung transplantations were performed. All pathological lung samples were systematically reviewed by one expert pathologist (C.D.). Hematoxylin eosin, picrosirius staining, and elastic van Gieson staining were routinely performed to characterize the morphology, the collagen content, and the elastin content, respectively. Lung function test results at diagnosis and follow-up were recorded. All available high-resolution CT (HRCT) scans of the chest were reviewed by one experienced chest radiologist (M.P.D.). All cases were collectively reviewed during a multidisciplinary discussion involving clinicians, radiologists, and pathologists in the Competence Center of Rare Pulmonary Diseases of Bichat Hospital.

For this retrospective, observational, noninterventional analysis of medical records, French law does not require specific approval by an internal review board or the consent of patients.

Results

We describe the clinical features of five women, which are summarized in Table 1.

Patient 1

A 47-year-old nonsmoking woman was referred for worsening dyspnea. She used to be employed at a swimming pool from age 20. Acute episodes of dyspnea with wheezing appeared 2 years after beginning the job. She received a diagnosis of asthma. At the time of the study, lung function tests showed a restrictive pattern; however, FEV_1 increased by 20% after salbutamol inhalation. Her medical condition gradually worsened. Chest HRCT showed extensive peribronchial consolidations almost exclusively involving the upper zones of the lung (Fig 1). The pleura and subpleural parenchyma appeared normal. Fiberoptic bronchoscopy was performed. BAL fluid (BALF) analysis showed a normal cellular distribution. Bronchial biopsy showed nonspecific inflammation. Transbronchial biopsy showed minimal fibrosis of the alveolar septa with excessive elastosis around the airways. Oral corticosteroids (prednisone, 0.5 mg/kg/day for 1 month) had no effect on lung function test results or CT abnormalities. A surgical lung biopsy (right upper and lower lobes) showed peribronchiolar fibroelastosis, as confirmed by elastic van Gieson stain (Fig 2). The pleura and the subpleural parenchyma were normal. There was mild nongranulomatosis inflammation with increased airway smooth muscle. We concluded that this patient with chronic asthma and a history of chlorine inhalation suffered from a purely airway-centered form of fibroelastosis.

Patient 2

A 40-year-old nonsmoking woman was referred for difficult-to-treat asthma. She had worked for several years on a farm. Her respiratory symptoms required daily oral corticosteroids. The patient had mild peripheral eosinophilia (Table 1). Repeated searches for antineutrophil cytoplasmic antibodies, *Aspergillus* infection, and *Aspergillus* sensitization were negative. Lung function tests showed an obstructive pattern without reversal after salbutamol inhalation. Chest HRCT revealed bronchial dilatation and bronchial wall thickening, with bronchial lumen distortion (Fig 1). Upper-lobe subpleural consolidations were minimal, as were peripheral ground-glass opacities bordered by curvilinear opacities, but bronchial abnormalities predominated. Abnormalities were almost exclusively in the upper lobes, which showed some volume loss. BALF contained 80,000 total cells/mL with 38% macrophages, 51% neutrophils, 6% lymphocytes, and 5% eosinophils. Bronchial biopsy showed mucous gland hyperplasia with thickened basal membrane. A surgical lung biopsy (right upper and lower lobes) showed mainly peribronchiolar elastosis. The pleura appeared slightly thickened. Besides airway-centered elastosis, signs of airway remodeling included excessive mucus with mucus plugs, mucous glands and goblet cell hyperplasia, eosinophilic infiltration, and epithelial