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Case report

# Emphysematous changes in hypersensitivity pneumonitis: A retrospective analysis of 12 patients

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ABSTRACT

*Introduction:* Emphysema is most commonly associated with smoking but also occurs in hypersensitivity pneumonitis (HP). The aim of this study was to further explore this relationship.

*Methods:* A retrospective, computer-assisted search was performed to identify patients with HP seen at Mayo Clinic in Rochester, Minnesota, from January 1997 through February 2014. Demographic, clinical, and imaging features were analyzed. Patients were excluded if they had a smoking history of 10 pack-years or more.

*Results:* Twelve patients (9 males) with HP and computed tomographic evidence of emphysema were identified. Ten were never smokers and 2 were ex-smokers. The median age at diagnosis was 47 (range, 29–77) years; median symptom duration was 2.2 (range, 0.2–13.4) years. The most common presenting symptoms were dyspnea (83%) and cough (67%). On pulmonary function testing, 6 patients (50%) had a restrictive defect, 2 (17%) had airflow obstruction, and 4 (33%) had an isolated reduction in diffusing capacity of lung for carbon monoxide. The severity of emphysema ranged from mild to severe to focal bullae. All patients had chronic hypersensitivity pneumonitis (CHP). Centrilobular emphysema was most commonly seen with coexistent paraseptal emphysema in 5 patients.

Emphysema was most frequent in the upper lung but could be seen in any lobe.

*Conclusion:* Emphysema can occur in patients with CHP independently of smoking history and exposure to specific types of antigens. Emphysematous changes seem to progress at a slower pace compare to reticulations/fibrosis.

## 1. Introduction

Hypersensitivity pneumonitis (HP) is a complex interstitial lung disease (ILD) caused by inhalation of and sensitization to an aerosolized environmental antigen [1]. These antigens include bacteria (eg, *Saccharopolyspora*, and *Thermoactinomyces*), fungi, mycobacteria, animal proteins (eg, avian antigens), and chemicals [2,3]. Patients with HP most commonly present with respiratory symptoms, although systemic symptoms may also be present. Consensus has not been reached on the criteria for diagnosing HP; the diagnosis relies on several factors, including history of antigen exposure, serologic presence of precipitating antibodies to causative antigens, clinical features, lymphocytosis on bronchoalveolar lavage, and supporting radiologic and pathologic abnormalities [2]. The clinical presentation of HP is divided into acute, subacute, and chronic forms, depending in part on the duration of exposure to the antigen [4]. Chronic HP (CHP), which results from continuous or recurrent low-level exposure to the offending antigen, is often associated with progressive pulmonary fibrosis.

The most commonly described radiologic findings in HP are ground-glass opacities, ill-defined centrilobular nodules, and focal areas of air trapping that result in mosaic attenuation and fibrosis [5]. Reports dating back to 1968 have described emphysematous changes in CHP, but the studies do not clearly delineate the pattern and extent of emphysema [6–11]. In addition, some of these studies did not adequately account for the smoking history, potentially confounding their results.

Our main goal was to investigate the pattern, severity, and distribution of emphysematous changes in HP along with their effects on pulmonary function. Since previous reports described emphysema mainly in farmers and bird breeders, we also explored whether this phenomenon is antigen specific.

## 2. Methods

### 2.1. Patient selection

A computer-aided search identified all adults at Mayo Clinic in

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**Abbreviations**

| | |
|---|---|
| $\alpha_1$-AT | $\alpha_1$-antitrypsin |
| CHP | chronic hypersensitivity pneumonitis |
| DLCO | diffusing capacity of lung for carbon monoxide ES, emphysema score |
| HRCT | high-resolution computed tomography |

Rochester, Minnesota, who received a diagnosis of HP from January 1, 1997, through February 28, 2014. Reports from computed tomography (CT) of the chest were reviewed for keywords *emphysema* and *emphysematous changes*. Patients with a smoking history of 10 pack-years or more were excluded from the study. The Mayo Clinic Institutional Review Board approved this study (IRB 13–007760). Patients were excluded if they did not provide written authorization for research use of their medical records.

### 2.2. Data extraction

Data extracted from the medical records included age, sex, smoking status, exposure history to known antigens, serologic evidence for HP, date of diagnosis, method of diagnosis, pathologic findings, spirometry results, findings from CT of the chest, treatment, outcome, and follow-up duration. A subspecialist thoracic radiologist (D.W.) reviewed all CT scans of the chest.

### 2.3. Diagnostic criteria of HP

All patients were seen by ILD experts in our ILD clinic. The multidisciplinary diagnosis of HP was made from the integration of several factors:

1. Presence of respiratory symptoms with or without the systemic symptoms of progressive dyspnea, dry cough, fatigue, and weight loss
2. History of exposure to a potential antigen [2,3].
3. Serologic presence of immunoglobulin G precipitating antibodies against a potential antigen [12].
4. Presence of at least 20% lymphocytes on bronchoalveolar lavage [12].
5. High-resolution CT (HRCT) scan supporting features of HP, including presence of ground-glass opacities and centrilobular nodules, and prominent air trapping or fibrosis predominantly in the upper or mid lung
6. Histologic findings of airway-centered interstitial lymphoplasmacytic infiltrates, poorly formed nonnecrotizing granulomas, bronchiolitis or usual interstitial pneumonia (UIP), or “bridging fibrosis” (ie, fibrotic net connecting bronchioles with each other and with the pleural/septal region)

In 10 of 12 patients, the diagnosis of HP was confirmed with lung biopsy. In the other 2, the diagnosis of HP was made from the combination of clinical, serologic, and CT of the chest findings.

### 2.4. Emphysema scoring

The scoring system used to assess emphysema was adapted from the COPDGene Study [13]. Each lung was divided into 3 zones: upper (above the carina), middle (between the carina and the inferior pulmonary veins), and lower (below the inferior pulmonary veins). The extent of emphysema as a percentage of lung volume within each zone was scored as 0 (absent), 1 ($\leq$5%), 2 (6%–25%), 3 (26%–50%), 4 (51%–75%), or 5 ($>$ 75%).

The patient's emphysema score (ES) was calculated by adding the numerical score for each lung zone. The predominant pattern of emphysema was recorded as centrilobular, paraseptal, panlobular, cicatricial or irregular, or bullae. When more than 1 morphologic type of emphysema was present, the less extensive type was recorded as a secondary pattern.

## 3. Statistical analysis

Categorical variables were compared between groups with the Fisher exact test. The Wilcoxon rank sum test was used to compare continuous variables between groups. *P* values less than .05 were considered statistically significant. Linear regression was used to assess the relationship between ES and pulmonary function test (PFT) data.

## 4. Results

Demographics and salient clinical features are summarized in Table 1. Most patients (75%) were men. At diagnosis, the median age was 47 (range, 29–77) years. Ten of 12 patients were never smokers; 1 ex-smoker had used a pipe for 20 years, and another ex-smoker had a smoking history of 5 pack-years. Ten of 12 patients were white; 1 was African American and another was Hispanic American. The median age between the onset of HP symptoms and the diagnosis of HP was 2.24 (range, 0.15–13.43) years. In 7 of 12 patients, the $\alpha_1$-antitrypsin ($\alpha_1$-AT) level was normal. An exposure history to known antigens associated with HP was elicited from 8 patients: 2 were farmers, 4 had exposure to avian antigens (2 to birds; 2 to down pillows or comforters), 1 was a potter in a home studio (with exposure to moldy clay), and 1 used a home steam shower (with exposure to mold). HP serology was positive for 6 of 10 tested patients.

The most common presenting symptoms were dyspnea (83%) and cough (67%), and one-third of the patients had lost weight. PFTs showed a restrictive pattern in 6 patients (50%), an isolated reduction in diffusing capacity of lung for carbon monoxide (DLCO) in 4 (33%), and an obstructive defect in 2 (17%) (Table 1). All patients had a reduced DLCO at HP diagnosis. Echocardiographic data were available for 8 of the 12 patients, and 2 had evidence of pulmonary hypertension (estimated right ventricular systolic pressure $>$ 50 mm Hg).

The mean (SD) HRCT patient emphysema score was 9.2 (5.5). The most common type of emphysema was centrilobular, with paraseptal emphysema present as a secondary pattern in 5 patients (Table 2 and Fig. 1).

Two patients presented with large bullae (Fig. 2). Panlobular emphysema was not observed. Emphysema had a predilection for the

**Table 1**
Demographic and clinical features of 12 patients with emphysematous changes and CHP.

| Characteristic | Value[a] |
|---|---|
| Male sex | 9 (75) |
| Age at HP diagnosis, median (range), y | 47 (29–77) |
| Presenting symptoms | |
| Dyspnea | 10 (83) |
| Cough | 8 (67) |
| Weight loss | 4 (33) |
| Exposure history—present | 8 (67) |
| HP serology[b] | |
| Positive | 6 (60) |
| Negative | 4 (40) |
| Pulmonary function test results | |
| Restrictive | 6 (50) |
| Isolated reduction in DLCO | 4 (33) |
| Obstructive | 2 (17) |

Abbreviations: DLCO, diffusing capacity of lung for carbon monoxide; HP, hypersensitivity pneumonitis.

[a] Unless otherwise indicated, values are number of patients (percentage).

[b] HP serology was performed for 10 of the 12 patients.