Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: May 31, 2024

Citation: Ajim A, Jabri H, et al., 2024. Hypersensitivity pneumonitis from Diagnosis to Treatment: A Cases Series with Literature Review, Medical Research Archives, [online] 12(5). https://doi.org/10.18103/mra.v12i5.5413

DOI
https://doi.org/10.18103/mra.v12i5.5413

ISSN: 2375-1924

CASE SERIES

Hypersensitivity pneumonitis from Diagnosis to Treatment: A Cases Series with Literature Review

A. Ajim*[1], H. Jabri[1], M. Chahbounia[1], W. Elkhattabi[1], N. Bougteb[1], H. Arfaoui[1], M. H. Afif[1], K. Rebbouh[2], N. Moussali[2], A. Merzem[2], H. Belgadir[2], O. Amriss[2], N. El Benna[2]

[1] Department of Respiratory Diseases 20 August 1953, University Hospital Center IBN Rochd, Casablanca, Morocco
[2] Department of Radiology 20 August 1953, university hospital IBN ROCHD, Casablanca, Morocco

***Corresponding author:** docteurasmaaajim@gmail.com

ABSTRACT:
Hypersensitivity pneumonitis (HP) classified as an interstitial lung disease is characterized by a complex immunological reaction of the lung parenchyma in response to repetitive inhalation of a sensitized allergen. The estimated worldwide incidence of hypersensitivity pneumonitis is extremely rare and highly dependent on climatic, geographical, occupational and industrial factors. It might be secondary to a domestic or professional exposure, usually occurs in people who work in places where there are high levels of dust, fungus, or molds. Long-term exposure can lead to lung inflammation and acute lung disease. Over time, the acute condition turns into long-lasting (chronic) lung disease. Thus, we distinguish 2 mains aspects fibrotic HP and Nonfibrotic HP. The diagnosis of HP maybe sophisticated especially in fibrotic form. The prognosis of this disease depends on early diagnosis with complete antigen avoidance and most often corticosteroid therapy.
This work aims to study the epidemiological, clinical, paraclinical aspects of hypersensitivity pneumonitis as well as therapeutic management, through a series of eight cases of HP carried out at the Pulmonology Department 20 August 1953, University Hospital Center IBN ROCHD, between January 2020 and January 2022, analyzed using a pre-established exploitation sheet. The average age of the patients studied was 51 years with a female predominance (sex-ratio M/F= 0.34). Domestic and occupational exposures of our patients were equal. The clinical symptomatology is dominated by almost constant dyspnea in all patients. Physical signs increased by crackles, objectified in 75% of patients. Computed tomography (CT) remains a great diagnostic contribution. Thus, allowing to have two categories of patients, depending on the presence or absence of signs of pulmonary fibrosis.
In our study, five patients had fibrotic HP, and three cases had non-fibrotic HP. Precipitins were positive. Plethysmography objectified a restrictive ventilatory disorder in 62.5%. All patients benefited from antigenic eviction with long-term corticosteroid therapy. The evolution was favorable in 87.5% of cases.

Introduction:

Hypersensitivity pneumonitis (HP), formerly known as extrinsic allergic alveolitis (EAA), are bronchopulmonary granulomatosis of immunological mechanism, caused by an exacerbated response to repeated inhalation of antigens, most often organic, to which the subject has been previously sensitized [1]. The most common and classic forms are Bird Breeders' Disease and Farmer's Lung Disease [2]. The diagnosis of HP is delicate, based on a set of arguments: exposure to an antigen, symptoms, imaging compatible with high-resolution chest computed tomography, lymphocytic alveolitis in bronchoalveolar lavage, associated or not with the presence of precipitating IgG antibodies (precipitins).

To date there is no internationally standardized criteria that could be applied, which make the diagnosis sophisticated and delayed [3]. However, the identification of HP cases is essential in order to provide to the patient the appropriate therapeutic strategy The therapeutic approach consists mainly of antigen avoidance and pharmacological treatment with corticosteroids/immunosuppressive drugs. In the majority of cases, this prevents unfavorable evolution. Systemic corticosteroid therapy is the first-line medical treatment for severe hypoxemic disease to avoid the development of fibrotic lesions. Antifibrotic therapy became the treatment of choice, after demonstration of the progressive nature of the pathology and failure of immunomodulatory/immunosuppressive therapies [2].

The prognosis of the disease depends closely on the early diagnosis and the implementation of an appropriate therapeutic strategy, which is a major challenge. Indeed, HP may be life-threatening in the short term due to the risk of acute respiratory failure. The chronic evolution towards fibrosis and consequently a chronic respiratory failure might be stoppable in case of early and effective management.

The aim of this work is to study the epidemiological, clinical, paraclinical, and therapeutic characteristics of hypersensitivity pneumonitis through a retrospective study spread over a period of 2 years, carried out at the Pulmonology Department 20 August 1953, University Hospital Center IBN ROCHD, Casablanca, Morocco.

Patients and methods:

This is a retrospective study of eight cases of hypersensitivity pneumonitis carried out at the Pulmonology Department 20 August 1953, University Hospital Center IBN ROCHD, between January 2020 and January 2022, analyzed using a pre-established exploitation sheet.

Inclusion criteria comprise: all patients over 18 years old, both sexes, hospitalized in our department.

Exclusion criteria include: patients under 18 years old. Patient with medical history of lung disease,
Statistical analyses were performed using Microsoft Excel software.

Results:

This is a retrospective descriptive study of a series of 8 cases of patients suffering from hypersensitivity pneumonitis. The average age of the patients studied was 51 years with a female predominance. Domestic and occupational exposures of our patients were equal. The table below summarizes the data from the eight observations.

			Average
AGE			51 years old
GENDER			The male/female sex-ratio : 0.34
PAST MEDICAL HISTORY	Occupational Exposure		50% (4 cases)
	Domestic Exposure		50% (4cas) (Pigeon+++)
	Toxic History	Smoking	75% (6 cases)
		Ex-smoker	25% (2 case)
	Pathological history	Flu-Like Syndrome	62.5% (5 cases)
		Chronic Bronchitis	25% (2 cases)
		AHT	12.5% (1 case)
		Diabetes	12.5% (1 case)

CLINICAL	Symptoms	Respiratory signs	dyspnea	100% (8 cases)
			Dry cough	62.5% (5 cases)
			Productive cough	25% (2 cases)
			Chest pain	25% (2 cases)
		Extra-respiratory symptoms	Deterioration of general condition	25% (2 cases)
			Fever	37.5% (3 cases)
	Physical signs	Crackling		75% (6 cases)
		Wheezing		37.5% (3 cases)
		Rhonchi		12.5% (1 case)
		Clubbing		50% (4 cases)
PARACLINICAL INVESTIGATIONS	Radiologic	Chest Xray	Syndrome interstitial	87.5% (7 cases)
			Normal	12.5% (1 case)
		CT scan	Ground glass opacity	75% (6 cases)
			Nodules /micronodules	62.5% (5 cases)
			Air trapping	50%(4 cases)
			Signs of Fibrosis	62.5% (5 cases)
			Bronchectasis	50%(4 cases)
			Traction	
			Septal thickening	62.5% (5 cases)
			Infiltrates Reticular	50%(4 cases)
			Honeycomb	12.5% (1 case)
	Bronchoscopy	Macroscopic aspect	Bronchial inflammation of the 1st degree	25% (2 cases)
			2nd degree inflammation	50%(4 cases)
			Normal	25% (2 cases)
		Bronchoalveolar lavage	Lymphocytic alveolitis,	50% (4 cases)
		Bronchoalveolar lavage	Macrophage alveolitis	12.5% (1 case)
			Neutrophilic Alveolitis	12.5% (1 case)
			Chronic Inflammation	75% (6 cases)
	Biology	Complete Blood Count	Lymphopenia	37.5% (3 cases)
		Precipitin	Anti-avian antibodies	87.5% (7 cases)
	Respiratory fonction	Plethysmography	Restrictive lung disease	62.5% (5 cases)
			Mixed Ventilatory defect	12.5% (1 case)
		DLCO test	Reduced	37.5% (3 cases)
Fibrosis	NonfiroticHP			37.5% (3 cases)
	Fibrotic HP			62.5% (5 cases)
Treatment	Antigenic eviction			100% (8 cases)
	Corticosteroid therapy			100% (8 cases)
Evolution	Favorable			87.5% (7 cases)
	Unfavourable			12.5% (1 case)

Discussion:

HP is a respiratory disease with varied clinical presentations, resulting from lymphocytic and frequently granulomatous, inflammation of the peripheral bronchi, alveoli and adjacent interstitial tissue, related to a non-IgE-mediated allergic reaction to numerous organic agents or low molecular weight chemicals present in the environment [4].

Respiratory signs are aspecific, misleading. They are often trivialized nevertheless they represent the chief complaint. In fact, in our series, dyspnea was the main symptom; followed by a dry cough in 62.5% (5 cases) of patients, and flu-like syndrome in 62.5% (5 cases) of patients, usually including of: fever, myalgias, arthralgias, headaches, rhinorrhea, often occurs a few (hours 4 to 8 hours) after a given exposure. This is consistent with those reported in various series of the literature [5, 6, 7].

According to several studies, including ours, the predominance of crackling on auscultation has been highlighted as the frequent physical sign found [7].

Extra-respiratory signs associated with HP are less frequent, non-specific and may point to other types of ILD, making diagnosis difficult.

On standard chest X-ray, several X-ray images may be suggestive but not specific of HP. However, its normality does not exclude diagnosis. However, it justifies further exploration if HP is suspected [8].

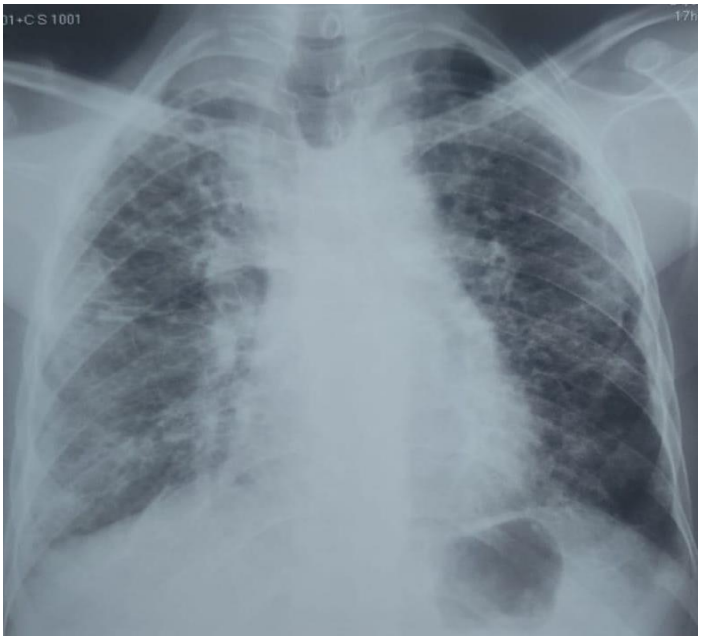


Figure 1: Chest X-ray faced: a retracted right lung, with a right apical pleural cuff, some right basal alveolar type opacities with left reticulomicronodular infiltrates.

The exploration of ILD makes systematic use of high-resolution computed tomography (HR-CT) in millimeter sections because of its very high sensitivity in the detection of parenchymal abnormalities.

In the specific context of HP, exploration should be carried out by two series without injection of contrast medium, one performed in deep inhalation, the other performed in prolonged exhalation [7, 9].
In Nonfibrotic hypersensitivity pneumonitis, diffuse ground-glass opacities and centrilobular nodules are mainly found [10]. On expiratory sections, areas of air trapping can also be identified, more or less associated with low vascularity. The latter abnormalities are related to distal obstructive bronchial involvement.

In fibrotic hypersensitivity pneumonitis, there is a variable association of irregular linear and reticular opacities, ground glass, and septal thickening [10]. More rarely, cysts may be associated with parenchymal lesions. Emphysematous forms have also been described, notably in farmer's lung [11].

In the most advanced forms, the presence of traction bronchiectasis and architectural distortion are possible. The honeycomb can also be observed the lungs of those with certain end-stage. It is then more rarely basal localized than in usual interstitial lung disease (UIP), a characteristic pattern of Idiopathic pulmonary fibrosis (IPF) [12].

This heterogeneity may delay the diagnosis and treatment. In almost half of the cases, it is not

possible to formally distinguish between Fibrotic Hypersensitivity Pneumonitis and other patterns such as IPF or non-specific interstitial lung disease (NIPS) [12].

In our series, chest CT was performed and judged to be abnormal in all patients, and the most common radiological appearance was the ground glass image in 75%, which is consistent with the results reported by other authors, including the series of Morell F and al. also the series of Santos, V and al.

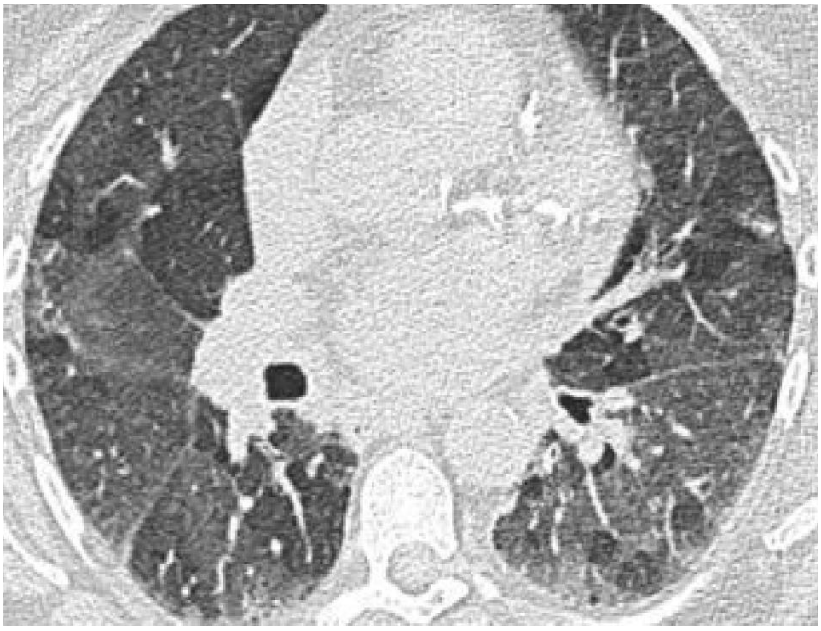
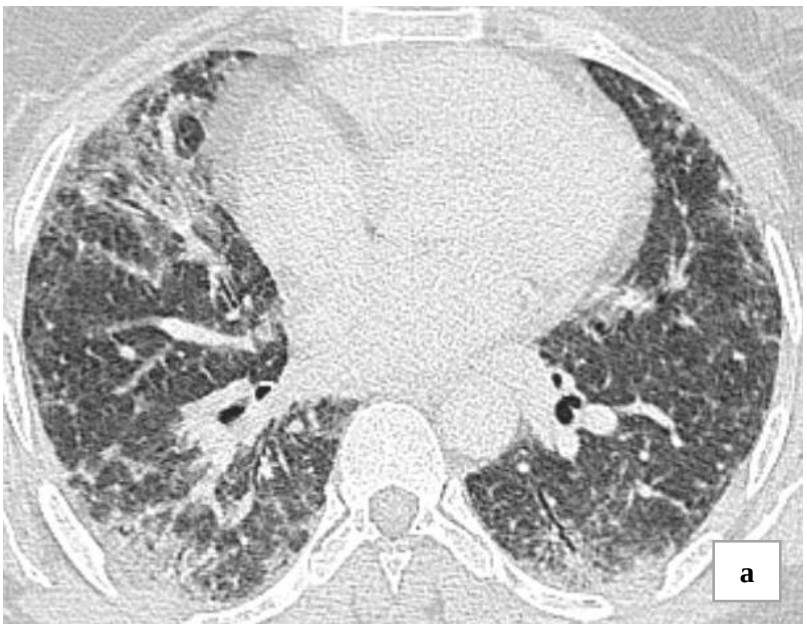


Figure 2: Chest CT scan (high resolution) in inspiration, millimeter section. heterogeneous ground glass areas: hypersensitivity pneumonitis related to mold exposure.



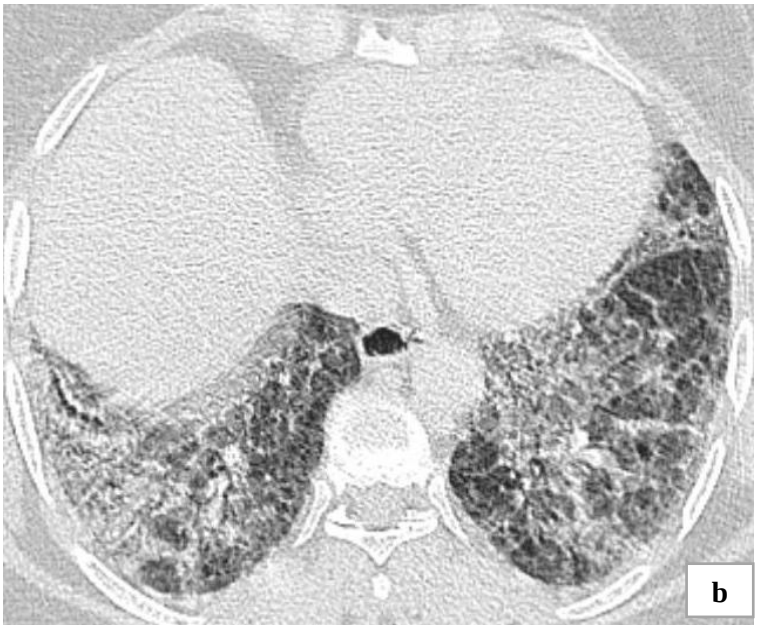


Figure 3 (a, b): Image of two axial CT sections of the parenchymal window, showing symmetrical bilateral ground glass opacity with bilateral micronodules with septal and intralobular cross-links.

The bronchoalveolar lavage is an important argument of the diagnosis of HP, when it typically shows hypercellularity with significant lymphocytosis usually exceeding 50%, with a decreased CD4+/CD8+ ratio (the latter is usually reversed in sarcoidosis). This can be influenced by many factors, including the duration of the disease, smoking status, and the presence or absence of fibrosis [13]. The bronchoalveolar lavage alone does not confirm or rule out the diagnosis of HP. Nor does it seem to have any particular prognostic value in this context [14].

In our study, hypercellularity was present in 75% of patients, with a predominance of lymphocyte alveolitis in 50% of cases.

The presence of IgG antibodies against specific antigens, or precipitin, is also an important marker but is not pathognomonic of HP. Their presence mean sensitization in a predisposed subject, which indicates often significant and prolonged exposure to an antigen. But it does not necessarily indicate the development of an HP.

The Nonfibrotic HP is associated with restrictive ventilatory disorder with a variable reduction in total and vital lung capacity, and a decrease in pulmonary compliance and CO diffusion capacity. This decrease in DLCO is the most interesting functional abnormality. It predicts oxygen desaturation during exercise. The existence of bronchial obstruction, especially distal obstruction, is common [15].

In our study, it is noted a predominance of restrictive ventilatory disorder found in 62.5% of cases (5 cases). Histological analysis may be very interesting in the diagnostic of ILD, by transbronchial biopsy or thoracoscopy. In the lack of signs in favor of another disease, the presence of the follow triad is specific to HP; Sparse poorly formed non-caseating granulomas and chronic inflammation are seen around the bronchioles with variable amounts of fibrosis. Pathologically this can appear similar to usual interstitial pneumonia (UIP) or fibrotic non-specific interstitial pneumonia (NSIP). Poorly formed granulomas and fibrosis centered around the small airways support HP over the alternate diagnosis. In advanced fibrosis, histologic changes become indistinguishable from UIP and may require clinical and radiographic correlation [16].

To date, there are no international guidelines for the treatment of HP [17]. Absolute avoidance of the suspected antigen is the first step in the management of HP. Systemic corticosteroid therapy is nevertheless considered to be the first-line medical treatment for severe hypoxemic disease, at an initial dose of 0.5 mg/kg/day associated to preventive measures. The immunomodulators are indicated in case of worsening or ineffectiveness of corticosteroid therapy. Antifibrotic: in case of pulmonary fibrosis or after failure of immunomodulatory treatments. Lung transplantation: are to be discussed in severe forms.

A recent study [18] involving the follow-up of 22 patients confirmed an excellent prognosis, with almost half of the subjects retaining moderate

bronchial obstruction and a decrease in DLCO test. Normalization of CT images is observed in 80% of cases after treatment.

In our study, 7 patients had a clear clinical improvement with a stable radiological appearance, and a clinical worsening was found in one patient, since antigenic avoidance was not respected.

Conclusion:

HP is a complex interstitial lung disease (ILD). The most common forms described in the literature are Bird fancier's lung and farmer's lung disease. Although relatively rare, HP is a heterogenous disease with various clinical and radiological appearance. Still underdiagnosed, especially the Fibrotic HP. The diagnosis of HP is complex, based on a range of clinical, radiological, immunological and histological arguments. After diagnosis, antigenic eviction is the rule whenever possible.

Systemic corticosteroid therapy is the first-line therapy to prevent the development of fibrotic lesions.

References:

1. Dalphin J-C. Pneumopathie D'hypersensibilite. Emc - Pneumol 2016;13(3):1–13 [Article 6-039-E-30]:41.
2. Chauvin, P., Kerjouan, M., Jego, P., Jouneau, S., & Lescoat, A. (2021). Mise Au Point : Pneumopathies D'hypersensibilite. La Revue De Medecine Interne .
3. M Girard , Y Lacasse, Y Cormier- Hypersentivity Pneumonitis.Allergy.2009 :64(3) :322-34.
4. Quirce S, Vvandenplas O, Campo P, Cruz MJ et AL6Ocuupational hypersensitivity pneumonitis : an EAACI position paper. Allergy. 2016 ; 71 (6) :765-79.
5. Santos, V., Martins, N., Sousa, C., Jacob, M., Padrão, E., Melo, N., … Morais, A. (2019). Hypersensitivity pneumonitis: Main features characterization in a Portuguese cohort. Pulmonology.
6. Hanak, V., Golbin, J. M., & Ryu, J. H. (2007). Causes and Presenting Features in 85 Consecutive Patients With Hypersensitivity Pneumonitis. Mayo Clinic Proceedings, 82(7), 812– 816.
7. Lacasse, Y., Selman, M., Costabel, U., Dalphin, J.-C., Morell, F., Erkinjuntti-Pekkanen, R.,
8. Cormier, Y. (2009). Classification of Hypersensitivity Pneumonitis. International Archives of Allergy and Immunology, 149(2).
9. Vasakova M, Morell F, Walsh S, Leslie K, Raghu G. Hypersensitivity pneumonitis: perspectives in diagnosis and management. Am J Respir Crit Care Med. 2017;196(6):680---9.
10. Chauvin, P., Kerjouan, M., Jégo, P., Jouneau, S., & Lescoat, A. (2021). Mise au point : pneumopathies d'hypersensibilité. La Revue de Médecine Interne.
11. Dias OM, Baldi BG, Pennati F, Aliverti A, Chate RC, Sawamura MVY, et al. Computed tomography in hypersensitivity pneumonitis: main findings, differential diagnosis and pitfalls. Expert Rev Respir Med 2018;12(1):5–13.
12. Dalphin J-C. Pneumopathie d'hypersensibilité. EMC - Pneumol 2016;13(3):1–13 [Article 6-039-E-30]:41.
13. Silva CIS, Müller NL, Lynch DA, Curran-Everett D, Brown KK, Lee KS, et al. Chronic Hypersensitivity Pneumonitis: Differentiation from Idiopathic Pulmonary Fibrosis and Nonspecific Interstitial Pneumonia by Using Thin-Section CT. Radiology 2008;246(1):288–97.
14. Adderley N, Humphreys CJ, Barnes H, Ley B, Premji ZA, Johannson KA. Bronchoalveolar Lavage FluidLymphocytosis inChronicHypersensitivity Pneumonitis: A Systematic Review and Meta-Analysis. Eur Respir J 2020 [20002]
15. Creamer AW, Barratt SL. Prognostic factors in chronic hypersensitivity pneumonitis. Eur Respir Rev 2020;29(156):190167.
16. Dalphin, J.-C. (2005). Pneumopathies d'hypersensibilité. EMC - Médecine, 2(1), 24–33.
17. Chandra D, Cherian SV. Hypersensitivity Pneumonitis. 2023 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 29763093.
18. Lacasse Y, Selman M, Costable U, Dalphin JC et AL,-Clinical diagnosis of hypersensitivity pneumonitis.Am J Respir Crit Care Med 2003 :168(8) :952-58.
19. Girard, M., E. Israël-Assayag, and Y. Cormier, 2009a, Mature CD11c(+) cells are enhancedin hypersensitivity pneumonitis. Eur Respir J, v. 34, p. 749-56.