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Hypersensitivity Pneumonitis

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Introduction

Hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis, is a term that describes a spectrum of allergic/inflammatory pulmonary disease that occurs after inhalation of fine particulate organic or inorganic material by a sensitized individual.[1,2,3] HP represents a very small percentage of interstitial lung diseases (ILD), reported between 1.5%-13%,[4] although this may be severely under represented as in some new series HP was the most common form of ILD.[5] This condition is difficult to diagnose, as the clinical symptoms are often nonspecific and the pathologic and radiologic imaging findings can often resemble other pulmonary conditions; including other small airways disease and ILD.[6,7] Classically, the condition is subdivided into 3 forms: acute, subacute, and chronic HP. It is important to note that in any given individual, HP demonstrates a spectrum of clinical, pathophysiologic, and imaging findings, with the stages of HP commonly overlapping with more than 1 phase present in an individual at a given time point. It is difficult, therefore, to determine the exact incidence and prevalence of HP in the world, as many individuals go undiagnosed or misdiagnosed. Only a small percentage of individuals exposed to an antigen will develop HP and for the majority of antigens this percentage is unknown. For well researched conditions, such as farmer's lung or pigeon breeder's lung, the incidence for development of HP has been reported as 4-170/10^3 farmers and 1-100/10^3 breeders respectively.[8-10] In addition, even with high index of suspicion, a careful examination of the patient's exposures, and a confirmed histologic biopsy, up to 40% of patients with HP will not have an identified causative antigen.[3,7]

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Antigens

More than 300 substances have been identified, which if inhaled as fine particles can cause HP (Table). These allergens can be divided into 3 broad groups: microbial agents, animal and plant proteins, and chemical agents. The microbes involved can be bacterial, fungal, or protozoan. One of the better known forms of microbial HP, farmer's lung, develops secondary to the inhalation of thermophili-cactinomycetes that grow in decomposing hay.[11] As this bacteria likes to grow in warm damp environments, it can also contaminate heating/cooling and humidification equipment, leading to the development of multiple cases of HP. Another form of microbial HP, known as hot tub lung, occurs secondary to inhalation of aerosolized *Mycobacterium avium* growing in the hot tubs.[12] Animal and plant proteins are common triggers for the development of HP. Bird fancier's lung develops secondary to inhalation of avian allergens, especially from bird droppings or feathers. While many types of birds can trigger this condition, pigeons, doves, and birds from the family Psittaciformes (including parakeets, cockatoos, and parrots) are the most commonly reported sources of allergen. In addition to live birds, HP can also develop as a response to plucked feathers, such as those in pillows and duvets.[13] Low-molecular weight chemicals are not a common source of HP, as they are typically not intrinsically allergenic and require an interaction with a host protein to form a compound that triggers HP.[3]Isocyanates used to create such products as upholstery and insulation materials, are the most commonly studied low-molecular weight chemicals to cause HP, occurring in 1% of workers who inhale this compound.[14]

Clinical Presentation

The acute form of hypersensitivity pneumonitis (HP) occurs 4-6 hours after exposure to a large quantity of allergen. Patients present with respiratory symptoms including shortness of breath, dry cough, and chest tightness, as well as systemic symptoms including fever, chills, and fatigue. With acute exposure, symptoms typically resolve within 12 hours, but may last for a few days. The subacute form HP typically

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Table Causes of Hypersensitivity Pneumonitis (HP)

	Allergens	Source(s) of Exposure
Microbial agents		
Bacterial	Thermophilicactinomycetes	Decomposing hay, humidifiers and water-based heating/cooling systems
	Nontuberculous mycobacteria	Hot tubs, warm water, metal-cutting fluid
	Klebsiella	
Fungal	Aspergillus	Moldy malt, cork dust
	Penicillium	Moldy cheese
Protozoan	Naegleriagruberi	Humidifier/air conditioners
Plant/Animal Proteins		
Animal	Birds	Avian proteins, including stool and feathers
	Mollusk shells	Button manufacturing
	Proteins in animal fur	Pet grooming, veterinary care
Plant	Soy bean	Food processing
	Coffee	Food processing
Low-molecular weight chemicals		
Chemical	Isocyanates	Polyurethane foam, varnish, lacquer
	Copper sulfate	Copper sulfate use

develops after recurrent acute allergen exposure events. Symptoms in these patients are similar to the acute form of the disease, however are typically less severe, characterized by deteriorating respiratory function with interposed repeat incidences of acute symptoms. Patients will complain of a gradually developing productive cough, shortness of breath, and chest pain, as well as systemic symptoms including fatigue, anorexia, and weight loss, with symptoms lasting weeks to months. The chronic form of HP typically occurs after long-term low-level antigen exposure and often causes more subtle symptoms than the acute or subacute forms. Patients typically complain of gradually progressing chronic respiratory symptoms, including shortness of breath and cough, with symptoms worsening when in the setting of the allergen exposure (eg, at work, around birds, etc.) and often have not experienced the symptoms related to an acute HP event. It is important to note that the clinical presentation of HP is highly dependent on the quantity of inhaled antigen and frequency of exposure events, with symptoms overlapping between the multiple forms of HP. In addition, as these symptoms are nonspecific and the antigen exposure may not be known, these patients often experience a delay in diagnosis.

Histopathology

Regardless of the inciting agent, the histologic findings of HP are the same, with the patterns of presentation varying with the stage of the disease. Histologic changes associated with HP appear to be relatively uniform in distribution throughout the lung; however discordant findings are sometimes encountered, leading to the suggestion that biopsies from different lobes should be considered. In addition, lung biopsy may be necessary to help differentiate chronic hypersensitivity pneumonia from other forms of diffuse ILD.

Biopsy in the setting of acute HP is not routinely done. When performed, the histopathology appears to be most consistent with neutrophilic infiltration of the respiratory bronchioles. In addition, diffuse alveolar damage may also be seen during this stage of HP.[7,15]

Subacute HP is characterized by granulomatous interstitial bronchiolocentric pneumonitis, with inflammation characterized by lymphocytes. The granulomas are non-necrotizing, small and characteristically poorly formed. In certain instances, the histologic features can be similar to features of nonspecific interstitial pneumonia (NSIP).In addition, thin-walled cysts can be seen in a small percentage of patients.[16]

Chronic HP is characterized by fibrotic changes with architectural distortion superimposed on the subacute findings. The classical triad of chronic HP are (1) bronchiolocentric cellular chronic interstitial pneumonia, (2) chronic bronchiolitis, and (3) non-necrotizing peribronchiolar interstitial granulomatous inflammation.[17] The pattern of chronic HP may mimic usual interstitial pneumonia (UIP), NSIP, or organizing pneumonia, with areas of fibrosis, subpleural honeycombing, and fibroblast foci identified at histopathology.[18] Interestingly, in a case-cohort study; 43% of patients previously diagnosed with idiopathic pulmonary fibrosis (IPF) had a subsequent diagnosis of chronic HP.[19]

Bronchoalveolar lavage is an additional method used to detect lung inflammation in the setting of HP. A lymphocyte predominance at BAL is typically seen, but is not diagnostic of this condition.

Imaging Features

HP presents with a variety of CT patterns including ground-glass opacities (GGO), centrilobular nodules (CLN), mosaic perfusion/air trapping, headcheese sign, reticular opacities, traction bronchiectasis, and traction bronchiolectasis, less commonly honeycombing, and rarely cysts, and

consolidation. The complexity of diagnosis increases as these imaging findings can be found in isolation or in a variety of combinations, often forming complex imaging features and patterns. In addition, the involvement of the pulmonary parenchyma can range from mild to severe, with the extent of the pathology typically dependent on the duration, and degree of antigenic exposure in the setting of individual responsiveness to the antigen.

The Fleischner Society recently published a consensus statement outlining an imaging classification system for IPF.[20] The American Thoracic Society/European Respiratory Society/Japanese Respiratory society/Latin American Thoracic Society jointly published a clinical practice guideline outlining a management strategy for the diagnosis of IPF.[21] The revisions in the 2018 guideline represent an improvement in the prior 2011 diagnostic criteria.[22] In both the consensus statement and clinical practice guideline, high-resolution computed tomography (HRCT) is an integral part of the diagnostic criteria as are multidisciplinary teams. HRCT techniques are described in a separate chapter. The proposed imaging classification system and the updated histopathologic classification system are parallel designations with discordance in the description of the third category (indeterminate for UIP pattern). Specifically designating lower lung zone predominance instead of nonspecific involvement in craniocaudal distribution of lung involvement shifts the "indeterminate for UIP" category towards "possible UIP" category., however both the consensus statement and the clinical practice guideline stress the importance of interdisciplinary teams in diagnosing IPF. This emphasis must be considered when evaluating for potential HP.

Though there are obvious challenges in developing a tailored differential diagnosis due to similarities in clinical, pathologic, and imaging presentations, these 2 pattern descriptions provide a framework for diagnosis and management of pulmonary fibrosis, including most of the typical cases of HP, and can be used to triage of patients who may need multidisciplinary conference discussions and possibly biopsy.[23]

The imaging appearance of HP is a direct reflection of the histopathologic findings of HP. The GGO correspond to the presence of diffuse lymphocytic interstitial pneumonitis and minor degrees of organizing pneumonia. The poorly defined CLN are caused by cellular bronchiolitis, peribronchiolar interstitial pneumonitis, or focal areas of organizing pneumonia.[7] The lobular areas of decreased attenuation and air trapping are due to small-airway disease including cellular bronchiolitis and/or constrictive bronchiolitis.[24,25] It is also known that certain CT features of ILDs such as honeycombing correspond to a clear histologic fibrosis, other findings can represent histologic inflammation and/or fibrosis including CLNs, traction bronchiectasis/bronchiolectasis, GGO/reticulations, depending on the clinical and pathologic context.[26-28]

When developing a differential diagnosis based on imaging findings, it is important to note that HP shares many similar imaging patterns with other common and uncommon interstitial and fibrotic lung diseases. Familiarity with the various imaging manifestations of HP is important for early diagnosis and proper management of these patients, especially in the era of new practice guidelines associated with antifibrotic medications targeting IPF, especially with regards to the clinically critical differences in treatment between the 2 entities, such as high-dose immunosuppressive agents used to treat chronic hypersensitivity pneumonitis (CHP), which are known to be harmful in treating IPF.[29-33]The following discussion of imaging patterns utilizes the imaging classification for IPF as a framework to categorize the complex imaging features of the various phases of hypersensitivity pneumonitis (HP).

Typical HP Pattern

According to our current pathophysiologic understanding of HP, a mid and upper lung predominant distribution of the above mentioned imaging findings is considered the "typical HP pattern," corresponding to the ILDcategory of "most consistent with a non-UIP diagnosis," regardless of underlying etiology, evolution of the disease process, or chronicity of the findings, including acute, subacute, and chronic HP.[20] This correlates with the "alternative diagnosis" pattern when utilizing the clinical practice guideline.[21]

HRCT imaging in the acute phase of hypersensitivity pneumonitis is seldom performed due to the characteristic clinical manifestations of this condition and the rapid resolution of the symptoms and imaging findings.[25,34] When imaged, acute HP typically demonstrates CT findings that mimic acute pulmonary edema. Variable degrees of GGO, air trapping, and normal lung parenchyma can be seen (Fig. 1). The juxtaposition of these 3 different densities is known as the headcheese sign, characterized by the high density GGO, low density air-trapping, and normal attenuation lung.[35] Numerous ill-defined small (<5mm) CLN can also be seen throughout both lungs, occasionally sparing the apex and base, see Figure 2.[25,36,37]

Confident diagnosis of subacute HP depends on the presence of a combination of GGO, poorly defined CLN, and mosaic attenuation on inspiratory images that is associated with air trapping on expiratory images.[25,36,37] Superimposition of reticular opacities on the background imaging appearance of subacute HP suggests the presence of chronic HP.[7]

Upper lobe predominant fibrosis with or without air-trapping on HRCT are also classic features of chronic HP and are not typically seen in UIP/IPF; however, radiologic differentiation between these entities is only possible in about 50% of cases.[33] Additional features of chronic HP include traction bronchiectasis, traction bronchiolectasis, and honeycombing, although subacute HP can have fibrotic components and chronic HP can be nonfibrotic on CT as well as histologic examination.[24,25,38-40] The findings of chronic HP can be seen in Figure 3.

As in other ILDs, acute exacerbation of chronic HP (Fig. 3) is also possible presenting with CT features of acute/subacute HP superimposed over the background of chronic HP.[41,42] This is not specific however as such combination of CT features can also be seen without acute exacerbation.[25,40]

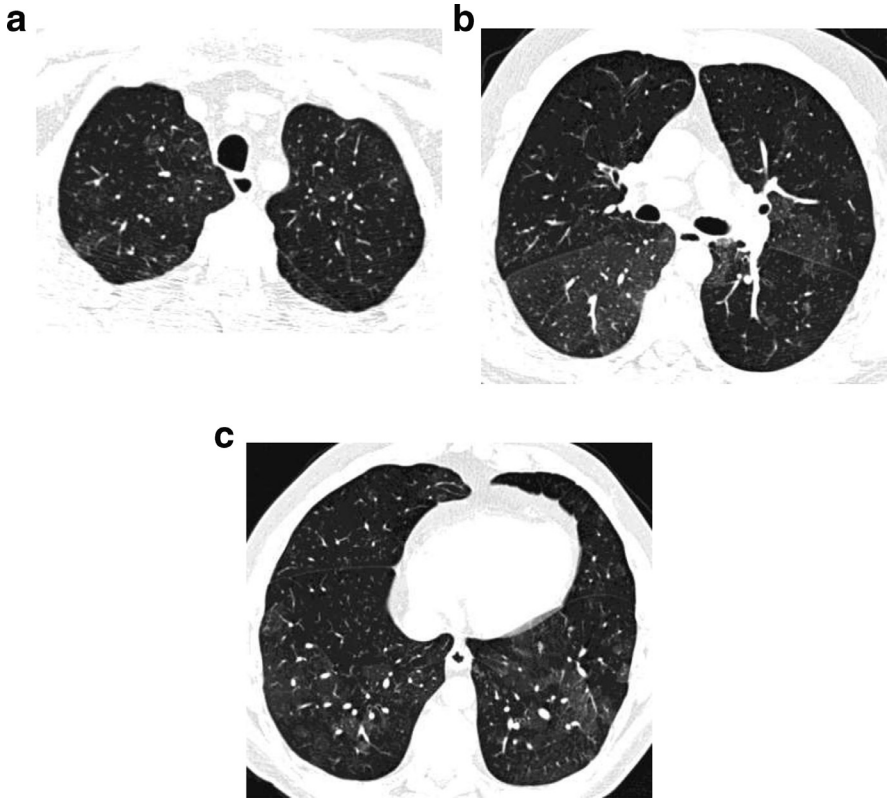

Figure 1 A 49 year-old-male with histopathology confirmed sub-acute HP, presumed to be from indoor hot tub use. CT images of the upper (a), mid (b), and lower lung (c) demonstrate ground glass opacities and mosaic pattern, a pattern that can be categorized as a non-UIP/alternative diagnosis and typical for Subacute HP.

Other Patterns Seen in HP

NSIP Pattern

HP can demonstrate atypical HRCT patterns that may be more typical for other ILDs. One such example is the cellular NSIP pattern, in which the lung involvement is peribronchovascular predominant in axial distribution, and with or without a craniocaudal gradient. This pattern is considered either "Indeterminate for UIP pattern" or "alternative diagnosis"[20,21] depending on the level of confidence in calling NSIP. This pattern can be caused by idiopathic NSIP, connective tissue disease (CTD), drug toxicity, and aspiration. When combined with bilateral and symmetrical presentation, this NSIP pattern of findings can be seen in the setting of HP.[25,43] In this setting, the GGO of HP usually are extensive, bilateral (in some patients, the distribution can be atypical, patchy, and/or asymmetric symmetrical).[25] Fine reticulation may be superimposed on a background of GGO, mimicking NSIP on high-resolution CT or at histologic examination.[7] Because of this, HP should always be considered a possible cause of a CT or histologic pattern of NSIP.[24,38] Importantly, chronic HP presenting with an NSIP pattern has a poor prognosis compared to idiopathic NSIP or NSIP related to CTD patients.[44]

UIP Pattern with HP Features

CHP can present with CT features that are indistinguishable from UIP/IPF. This is especially true when there is evidence of lower lung and peripheral predominant fibrosis, such as reticulation, traction bronchiectasis/bronchiolectasis, and honeycombing coexisting with substantial degree of features inconsistent with UIP including GGO and mosaic perfusion/air trapping. CHP should also be considered if there is diffuse or patchy craniocaudal distribution of fibrosis or if there is no clear craniocaudal gradient and there are superimposed features that are indeterminate for UIP or point toward an alternative diagnosis. If the fibrosis is mid-lung predominant, HP may be considered.[45]

Organizing Pneumonia Pattern

Presence of consolidation in a peribronchovascular and or peripheral distribution has been described in HP. These opacities correspond to areas of organizing pneumonia at histopathology (Fig. 4). Needless to say this pattern can be seen in cryptogenic organizing pneumonia or organizing pneumonia from other causes such as drug toxicity, CTD, toxic fume inhalations, and eosinophilic pneumonia

Sarcoidosis Pattern

The typical distribution of HP overlaps with that of sarcoidosis, which is also an upper lung predominant process associated with HRCT features of variable degree of mosaic perfusion/attenuation and air trapping. In some cases, presence of GGO or the lack of typical perilymphatic nodules seen in sarcoidosis can result in a pattern very similar to what we see in acute or subacute HP. In addition, sarcoidosis

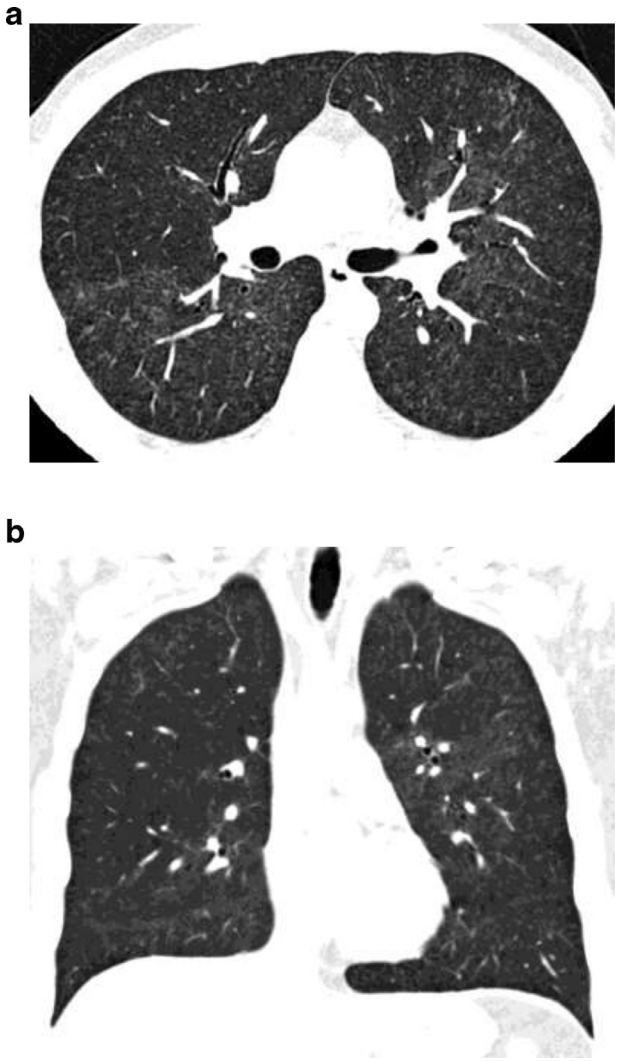

Figure 2 Axial CT image (a) and a coronal reformatted image (b) in a never smoker with a clinical diagnosis of HP demonstrates centrilobular ground glass attenuation nodules (also described sometimes as poorly defined centrilobular nodules).

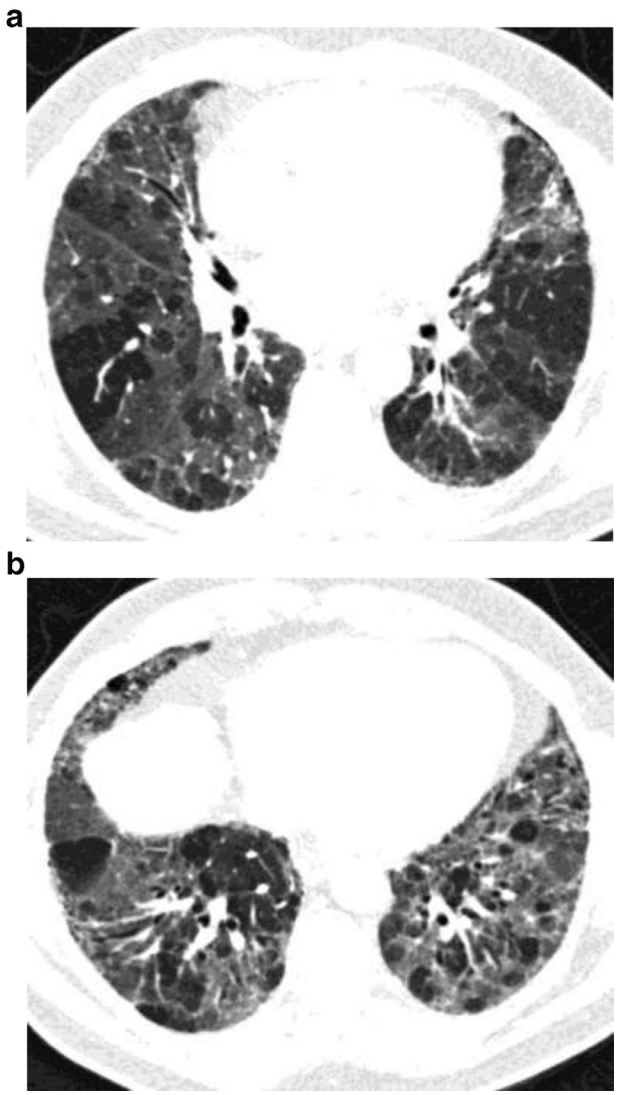

Figure 3 CT images (a and b) of a patient who presented with acute shortness of breath and previously known to have mild chronic dyspnea clinically diagnosed to have HP from birds. A classic headcheese pattern is present, however lower lung predominance was atypical. In addition there are areas of traction bronchiectasis and cyst formation indicating possible evolution into chronic HP.

can show GGO as a predominant finding on HRCT, however this is a rare occurrence. In addition, the headcheese sign has been described in patients with sarcoidosis. In a recent analysis of patients with both ILD and moderate to severe air trapping, 29% of patients had sarcoidosis, and 10% had HP.[46] Both sarcoidosis and HP can show fibrosis that spares the lung bases and involve the central lung. The main distinguishing imaging feature that specifically suggests sarcoidosis is a perilymphatic distribution of nodules and a peribronchovascular distribution of fibrosis.[46]

Emphysema Pattern

Patients with chronic farmer's lung, including lifelong nonsmokers, tend to develop a HP pattern of lung injury that resembles emphysema more than interstitial fibrosis as its dominant feature.[47] A recent study of 12 patients did demonstrate emphysema in patients without history of smoking but with chronic HP.[48]

Probable UIP pattern

When HP demonstrates lower lung and peripheral predominant distribution like fibrotic NSIP without coexistent extensive typical features of HP, such as GGO, CCN, mosaic attenuation/perfusion, and air trapping, the imaging pattern can appear closer to a "probable UIP" pattern, as can be seen in IPF, CTD, drug toxicity, idiopathic NSIP, and aspiration.[49] Importantly, 1 of 3of cases of HP will have lower lung predominance.[39] The majority of patients with HP, however, demonstrate some features inconsistent with UIP such as mosaic attenuation and air trapping particularly when present in relatively spared/nonfibrotic lung.[39] The confident identification of air-trapping diminishes, however, as the features of lung fibrosis becomes more extensive and coarser and more in keeping with the typical UIP pattern.[26] In a recent study,

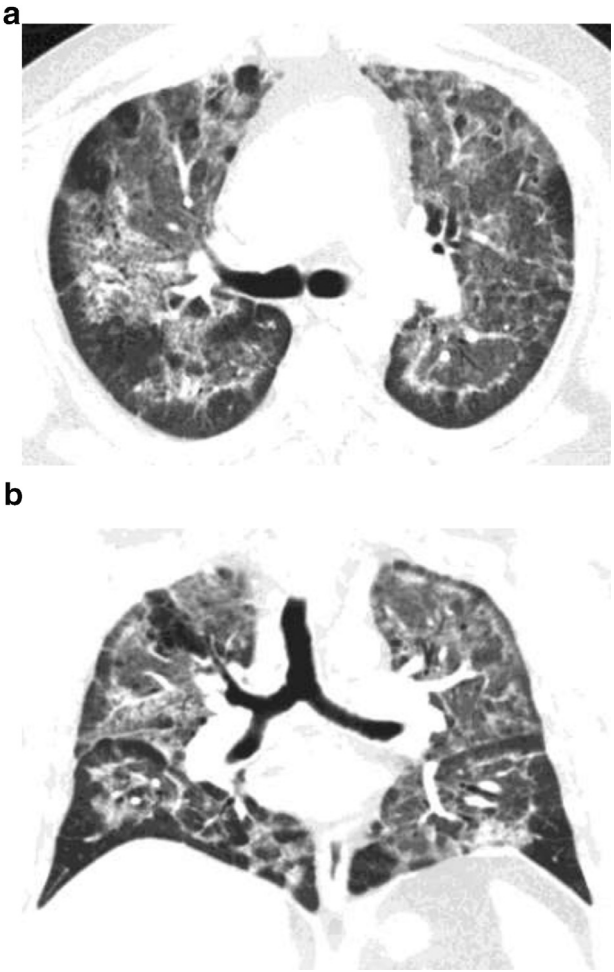

Figure 4 Axial CT (a) and coronal reformat (b) of the chest in this patient who was confirmed to have HP on histology, shows central lung predominant ground glass opacity and consolidation with a reverse halo pattern in some areas that is typical for organizing pneumonia.

mosaic attenuation or air trapping was the source of CT-pathologic discordance in 72% of cases with a final diagnosis of IPF.[50] In some patients, the GGOs of HP may be patchy or asymmetric, subtle and superimposed with subpleural fine reticulation in the dorsal regions of lower lobes and can be interpreted as normal dependent density on supine CT.[7]

UIP Pattern without HP Features

When HP demonstrates lower lung and peripheral predominant distribution, with honeycombing, but without the typical additional imaging findings of HP, this imaging pattern will correspond to a "UIP" pattern. If a UIP pattern is identified in a younger patient, HP, collagen vascular disease, or familial pulmonary fibrosis should be strongly considered.[22] In some cases, radiologic separation of CHP from UIP/IPF is possible in only about 50% of cases.[33]

The reticular pattern, traction bronchiectasis and honeycombing occur more frequently in patients who have fibrotic CHP compared with patients who have nonfibroticCHP.[26] It has been shown that in the CHP population, patients with a UIP pattern ground-glass opacity and air trapping is less often seen, and lower lobe volume loss, traction bronchiectasis and reticular pattern were more often present when compared with those without UIP.[26] The prevalence of honeycombing in CHP on HRCT ranges from 15% to 69%.[51,45,52]

Conclusion

The ILDs have been classified according to clinical, HRCT and pathologic patterns, which are shown to be congruent with each other and has been used successfully for diagnosis and management of patients. However, diagnostic and management challenges still exist for the cases that present with atypical or poorly defined and/or overlapping features and this affects the morbidity and survival of these patients.

In this review we aimed to present a concise description of typical and atypical imaging features of hypersensitivity pneumonitis. A successful consensus on potential future diagnostic criteria regarding hypersensitivity pneumonitis will require an adequately performed HRCT, including supine inspiratory and expiratory images and prone inspiratory images suspended at the fullest lung capacity possible. When the imaging pattern is less typical, a careful review of potential environmental exposures may help suspect the diagnosis early enough to prevent advancement to chronic HP.

References

1. Stankus RP, Morgan JE, Salvaggio JE: Immunology of hypersensitivity pneumonitis. Crit Rev Toxicol 11:15-32, 1982
2. Lynch DA, Rose CS, Way D, et al: Hypersensitivity pneumonitis: Sensitivity of high-resolution CT in a population-based study. AJR Am J Roentgenol 159:469-472, 1992
3. Lacasse Y, Girard M, Cormier Y: Recent advances in hypersensitivity pneumonitis. Chest 142:208-217, 2012
4. Thomeer MJ, Costabe U, Rizzato G, et al: Comparison of registries of interstitial lung diseases in three European countries. Eur Respir J Suppl 32:114s-118s, 2001
5. Singh S, Collins BF, Sharma BB, et al: Interstitial Lung Disease in India. Results of a Prospective Registry. Am J Respir Crit Care Med 195:801-813, 2017
6. Travis WD, Costabel U, et al: An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med 188:733-748, 2013
7. Silva CI, Churg A, Müller NL: Hypersensitivity pneumonitis: Spectrum of high-resolution CT and pathologic findings. AJR Am J Roentgenol 188:334-344, 2007
8. Demedts M, Wells AU, Antó JM, et al: Interstitial lung diseases: An epidemiological overview. Eur Respir J Suppl 32:2s-16s, 2001
9. Gruchow HW, Hoffmann RG, Marx JJ, et al: Precipitating antibodies to farmer's lung antigens in a Wisconsin farming population. Am Rev Respir Dis 124:411-415, 1981
10. Christensen LT, Schmidt CD, Robbins L: Pigeon breeders disease. A prevalence study and review. Clin Allergy 5:417-422, 1975
11. Cano-Jiménez E, Acu~na A, Botana MI, et al: Revisión de la enfermedad del pulmón de granjero. Arch Bronconeumol 52:321-328, 2016
12. Hanak V, Kalra S, Aksamit TR, et al: Hot tub lung: Presenting features and clinical course of 21 patients. Respir Med 100:610-615, 2006

13. Chan AL, Juarez MM, Leslie KO, et al: Bird fancier's lung: A state-of-the-art review. Clin Rev Allergy Immunol 43:69-83, 2012
14. Nakashima K, Takeshita T, Morimoto K: Occupational hypersensitivity pneumonitis due to isocyanates: Mechanisms of action and case reports in Japan. Ind Health 39:269-279, 2001
15. Selman M, Pardo A, King TE: Hypersensitivity pneumonitis: Insights in diagnosis and pathobiology. Am J Respir Crit Care Med 186:314-324, 2012
16. Franquet T, Hansell DM, Senbanjo T, et al: Lung cysts in subacute hypersensitivity pneumonitis. J Comput Assist Tomogr 27:475-478, 2003
17. Myers JL: Hypersensitivity pneumonitis: The role of lung biopsy in diagnosis and management. Modern Pathol 25(Supp 1):S58-S67, 2012
18. Churg A, Sin DD, Everett D, et al: Pathologic patterns and survival in chronic hypersensitivity pneumonitis. Am J Surg Pathol 33:1765-1770, 2009
19. Morell F, Villar A, Montero MÁ, et al: Chronic hypersensitivity pneumonitis in patients diagnosed with idiopathic pulmonary fibrosis: A prospective case-cohort study. Lancet Respir Med 1:685-694, 2013
20. Lynch DA, Sverzellati N, Travis WD: Diagnostic criteria for idiopathic pulmonary fibrosis: A Fleischner Society White Paper. Lancet Respir Med 6:138-153, 2018
21. Raghu G, Remy-Jardin M, Myers JL, et al: Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med 198:e44-e68, 2018
22. Raghu G, Collard HR, Egan JJ, et al: An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: Evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med 183:788-824, 2011
23. Elicker BM, Jones KD, Henry TS, et al: Multidisciplinary approach to hypersensitivity pneumonitis. J Thorac Imaging 31:92-103, 2016
24. Travis WD, Colby TV, Koss MN, et al: Idiopathic interstitial pneumonitis and other diffuse parenchymal lung diseases. Atlas of Nontumor Pathology Non-Neoplastic Disorders of the Lower Respiratory Tract. Washington, DC: American Registry of Pathology and the Armed Forces Institute of Pathology, 115-123, 2002
25. Hansell DM, Wells AU, Padley SP, et al: Hypersensitivity pneumonitis: Correlation of individual CT patterns with functional abnormalities. Radiology 199:123-128, 1996
26. Sahin H, Brown KK, Curran-Everett D, et al: Chronic hypersensitivity pneumonitis: CT features comparison with pathologic evidence of fibrosis and survival. Radiology 244:591-598, 2007
27. Akira M, Sakatani M, Ueda E: Idiopathic pulmonary fibrosis: Progression of honeycombing at thin-section CT. Radiology 189:687-691, 1993
28. Terriff BA, Kwan SY, Chan-Yeung MM, et al: Fibrosingalveolitis: Chest radiography and CT as predictors of clinical and functional impairment at followup in 26 patients. Radiology 184:445-449, 1992
29. Raghu G, Rochwerg B, Zhang Y, et al: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of idiopathic pulmonary fibrosis. An update of the 2011 clinical practice guideline. Am J Respir Crit Care Med 192:e3-e19, 2015
30. Vasakova M, Morell F, Walsh S, et al: Hypersensitivity pneumonitis: perspectives in diagnosis and management. Am J Respir Crit Care Med 196:680-689, 2017
31. Salisbury ML, Myers JL, Belloli EA, et al: Diagnosis and treatment of fibrotic hypersensitivity pneumonitis: Where we stand and where we need to go. Am J Respir Crit Care Med 196:690-699, 2017
32. Molyneaux PL, Maher TM: Time for an International Consensus on Hypersensitivity Pneumonitis. A Call to Arms. Am J Respir Crit Care Med 196:665-679, 2017
33. Churg A, Bilawich A, Wright JL: Pathology of Chronic Hypersensitivity Pneumonitis. What Is It? What are the diagnostic criteria? Why do we care? Arch Pathol Lab Med 142:109-119, 2018
34. Mohr LC: Hypersensitivity pneumonitis. Curr Opin Pulm Med 10:401-411, 2004
35. Chung MH, Edinburgh KJ, Webb EM, et al: Mixed infiltrative and obstructive disease on high-resolution CT: Differential diagnosis and functional correlates in a consecutive series. J Thorac Imaging 16:69-75, 2001
36. Tateishi T, Ohtani Y, Takemura T, et al: Serial high-resolution computed tomography findings of acute and chronic hypersensitivity pneumonitis induced by avian antigen. J Comput Assist Tomogr 35:272-279, 2011
37. Okada F, Ando Y, Yoshitake S, et al: Clinical/pathologic correlations in 553 patients with primary centrilobular findings on high-resolution CT scan of the thorax. Chest 132:1939-1948, 2007
38. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. Am J Respir Crit Care Med 165:277-304, 2002
39. Silva CI, Müller NL, Lynch DA, et al: Chronic hypersensitivity pneumonitis: Differentiation from idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia by using thin-section CT. Radiology 246:288-297, 2008
40. Patel RA, Sellami D, Gotway MB, et al: Hypersensitivity pneumonitis: Patterns on high-resolution CT. J Comput Assist Tomogr 24:965-970, 2000
41. Collard HR, Richeldi L, Kim DS, et al: Acute exacerbations of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 176:636-643, 2007
42. Miyazaki Y, Tateishi T, Akashi T, et al: Clinical predictors and histologic appearance of acute exacerbations in chronic hypersensitivity pneumonitis. Chest 134:1265-1270, 2008
43. Kligerman SJ, Groshong S, Brown KK, et al: Nonspecific interstitial pneumonia: Radiologic, clinical, and pathologic considerations. RadioGraphics 29:73-87, 2009
44. Nunes H, Schubel K, Piver D, et al: Nonspecific interstitial pneumonia: survival is influenced by the underlying cause. Eur Respir J 45:746-755, 2015
45. Adler BD, Padley SP, Müller NL, et al: Chronic hypersensitivity pneumonitis: High-resolution CT and radiographic features in 16 patients. Radiology 185:91-95, 1992
46. Miller WT, Chatzkel J, Hewitt MG: Expiratory air trapping on thoracic computed tomography. A diagnostic subclassification. Ann Am ThoracSoc 11:874-881, 2014
47. Cormier Y, Brown M, Worthy S, et al: High-resolution computed tomographic characteristics in acute farmer's lung and in its follow up. Eur Respir J 16:56-60, 2000
48. Baqir M, White D, Ryu JH: Emphysematous changes in hypersensitivity pneumonitis: A retrospective analysis of 12 patients. Respir Med Case Rep 24:25-29, 2018
49. Ohtani Y, Saiki S, Kitaichi M, et al: An application of the 2002 ATS/ERS consensus classification of the idiopathic interstitial pneumonias. Thorax 60:665-671, 2005
50. Yagihashi K, Huckleberry J, Colby TV, et al: Radiologic pathologic discordance in biopsy-proven usual interstitial pneumonia. Eur Respir J 47:1189-1197, 2016
51. Buschman DL, Gamsu G, Waldron JA, et al: Chronic hypersensitivity pneumonitis: Use of CT in diagnosis. AJR Am J Roentgenol 159:957-960, 1992
52. Lynch DA, Newell JD, Logan PM, et al: Can CT distinguish hypersensitivity pneumonitis from idiopathic pulmonary fibrosis? Am J Roentgenol 165:807-811, 1995