Hypersensitivity Pneumonitis

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21.1 Overview

Hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis (EAA), is a group of non-asthmatic allergic lung diseases characterized by diffuse interstitial changes of lung and caused by susceptible individuals' repeated exposure to various allergens in the environment.

The clinical manifestations of hypersensitivity pneumonitis are complex, with different courses of disease, occult onset, and diverse etiological factors. The disease can occur at any age, mainly in middle-aged people. The incidence rate of male is significantly higher than that of female [1, 2], the mortality rate of male is higher than that of female, and the mortality rate tends to increase with age. Smokers are rare in hypersensitivity pneumonitis patients [3]. The types of hypersensitivity pneumonitis are closely related to the types of pathogens, patients' living and working environment.

Antigens causing hypersensitivity pneumonitis include microbial antigens, animal and plant antigens, and low molecular weight compounds. Microbial antigens include bacteria, fungi, or protozoa. Animal and plant antigens mainly include protein and pollen in bird serum, feces, and feathers [4, 5]. Common low molecular weight compounds include isocyanates [6, 7]. The most common antigens of hypersensitivity pneumonitis are poultry antigens and microbial agents. Farmers' lung disease is a typical type of hypersensitivity pneumonitis, which is caused by farmers inhaling spores of thermophilic actinomycetes or Streptomyces thermohygroscopicus from moldy hay. This disease mostly occurs in late winter and regions with heavy rainfall or poor winter conditions [8].

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21.2 Pathological Manifestations

Pathological manifestations include usual interstitial pneumonia or peripheral bronchiolar fibrosis. The lesions are mainly distributed around bronchi or manifested as bridging fibrosis. Adjacent alveoli may be complicated with bronchiolar metaplasia, and the interstitium is accompanied by a small amount of loose granuloma and multinucleated giant cells, mainly lymphocyte exudation. Cellular bronchiolitis (airway central inflammation) and scattered non-caseous necrotizing granuloma are characteristic pathological changes [9]. Traditionally, hypersensitivity pneumonitis includes three stages, namely acute stage, subacute stage, and chronic stage. Long-term exposure to antigens can lead to irreversible fibrosis. The histological features of acute hypersensitivity pneumonitis are diffuse pulmonary congestion and edema and alveolar exudation caused by inflammatory cell infiltration and vasculitis in pulmonary parenchyma, neutrophils infiltrating respiratory bronchioles and alveoli, sometimes accompanied by diffuse alveolar damage and chronic interstitial pneumonia. Subacute hypersensitivity pneumonitis is mainly manifested as cellular bronchiolitis, non-caseous granuloma, and bronchointerstitial pneumonia, and some of them may be accompanied by organizing pneumonia (OP) [9].

21.3 Imaging Manifestations

1. X-ray: Chest radiograph may be normal or show diffuse interstitial fibrosis. The lesions often show bilateral plaques or nodular infiltration shadows, thickened lung markings, or small acinar changes. Hilar lymphadenectasis and pleural effusion are rare.
2. CT: Especially HRCT is of great value in diagnosing the type and extent of lesions.
   (a) Acute hypersensitivity pneumonitis: Both lungs show ground-glass changes or patchy, agglomerate,

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cloud flocculent lung consolidation shadows, with blurred edges (Fig. 21.1). The density and distribution are uneven, mostly in the middle and upper lung fields. The lesions change significantly in a short time and are migratory: one lesion can be absorbed in a short time, but another new lesion occurs elsewhere. After disconnecting from the contact environment, the hyperdensities can be absorbed or cannot be absorbed within 1 month or several months [10].

(b) Subacute hypersensitivity pneumonitis: Diffuse centrilobular nodules can be found in both lungs [11], mostly in middle and lower lung fields, with a size of 2–4 mm, medium density, and blurred edges (Fig. 21.2); patchy ground-glass opacities [12]; and "air trap" sign and pulmonary cystic changes, namely mosaic attenuation and air retention [13]. Centrilobular nodular opacities are the manifestation of bronchiolitis. Ground-glass opacities are the manifestation of lymphocytic interstitial pneumonia. "Air trap" sign and pulmonary cystic changes are the result of bronchiolitis and obstruction. Centrilobular nodules and ground-glass opacities are typical changes of hypersensitivity pneumonitis, and subacute hypersensitivity pneumonitis is characterized by centrilobular nodules.

(c) Chronic hypersensitivity pneumonitis: Pulmonary interstitial fibrosis occurs, but it often coexists with active lesions. Fibrosis mainly includes interstitial thickening in lobules, interlobular septum thickening and irregularity, honeycomb changes, and traction

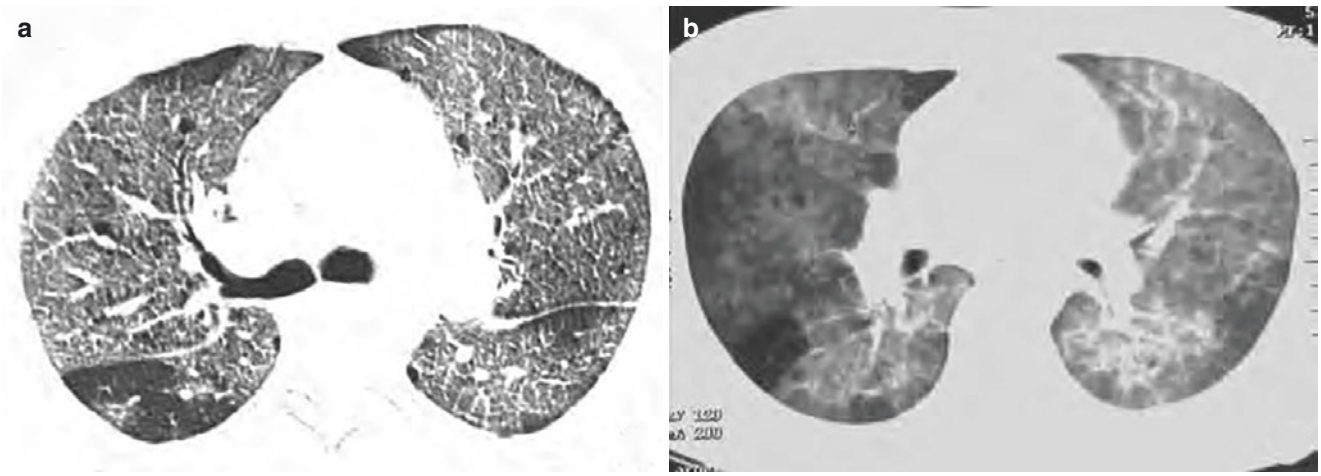

Fig. 21.1 Hypersensitivity pneumonitis (I). (**a**) CT lung window showed large patchy ground-glass opacities in both lungs, with diffuse distribution and (**b**) large patchy consolidation of both lungs with blurred edges

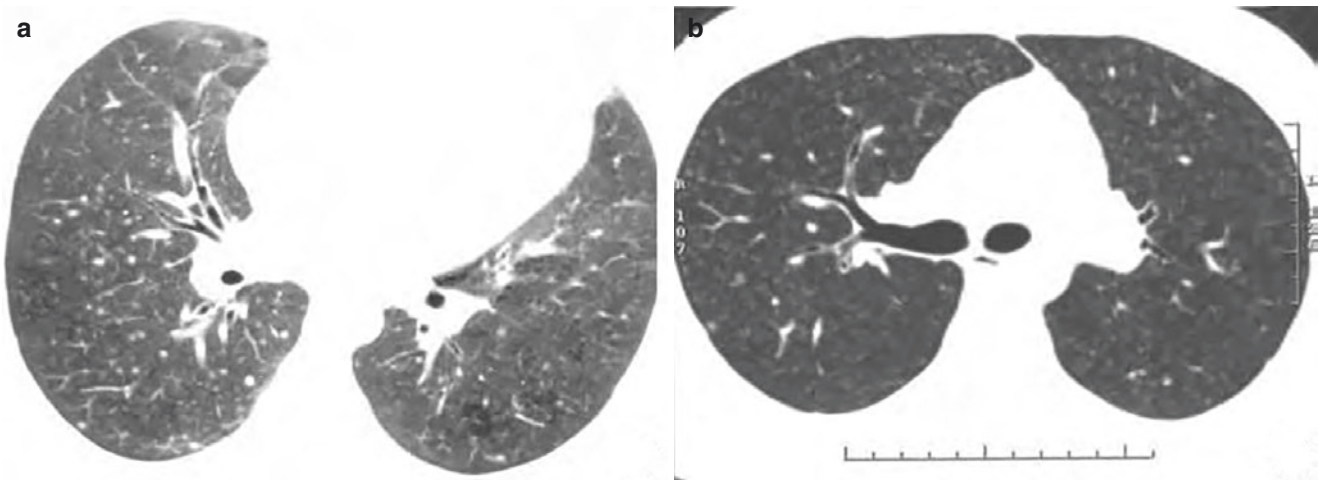

Fig. 21.2 Hypersensitivity pneumonitis (II). (**a** and **b**). CT lung window showed scattered miliary nodules and small patchy ground-glass opacities with blurred edges in the lung

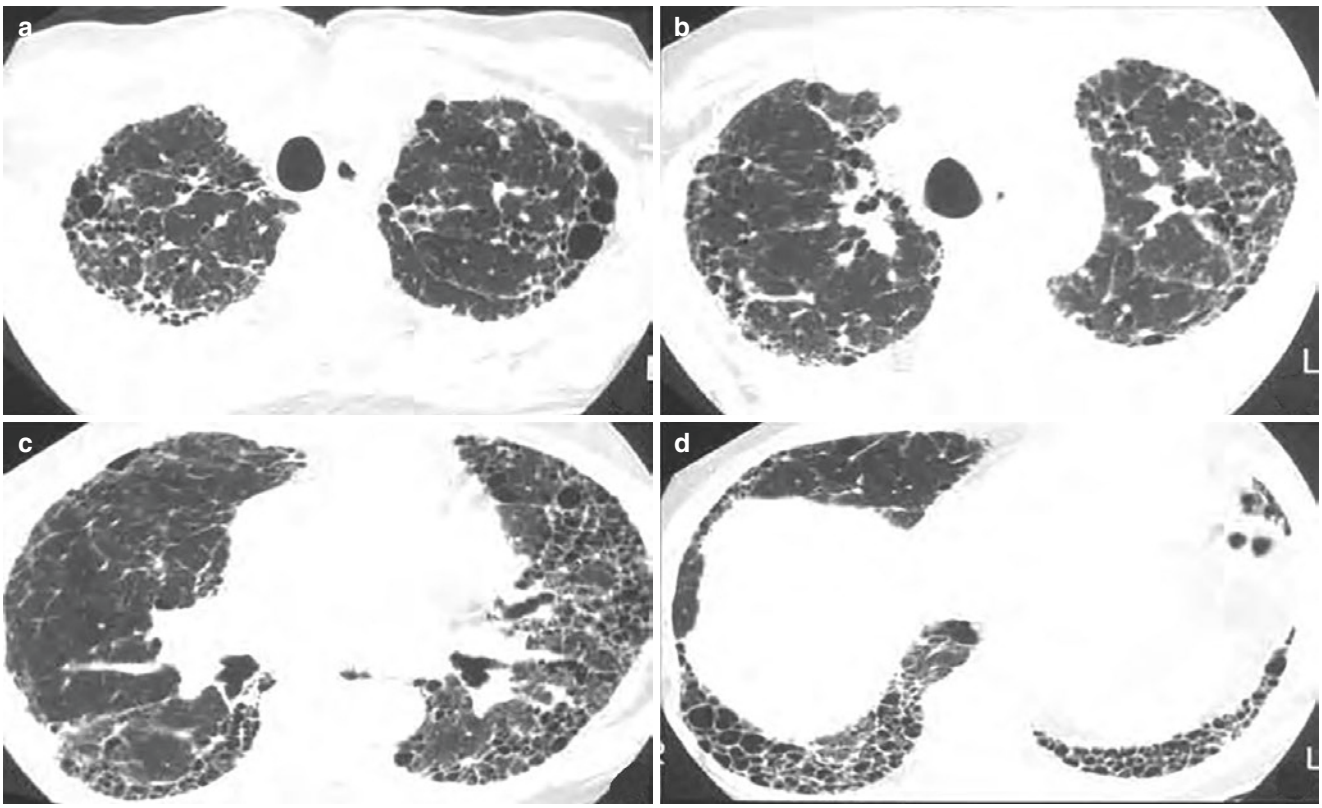

Fig. 21.3 Hypersensitivity pneumonitis (III). (**a**–**d**) CT lung window showed thickened interlobular septa and honeycomb changes in the subpleural area of both lungs

bronchiectasis (Fig. 21.3). Fibrosis mostly involves the middle and lower lungs but generally does not involve the basal part of the lung or is randomly distributed [14]. Atelectasis, emphysema, and pleural thickening may occur in severe cases [15, 16].

21.4 Diagnostic Key Points

1. Manifestations include diffuse patchy ground-glass opacities, subacute lobular nodules, and air retention. Chronic hypersensitivity pneumonitis is manifested as fibrosis, peripheral reticular opacities, structural disorder, traction bronchiectasis, and honeycomb shadow, usually not distributed in the lower lobe, which can indicate this disease.
2. Physical examination shows interstitial lung disease, with symptoms corresponding to hypersensitivity pneumonitis, recurrent onsets, and other clinical features, and excludes other lung diseases with similar symptoms.
3. Detailed inquiry includes medical history, especially the history of exposure to environment, occupation, and antigens, antigen components in family and daily living environment should also be considered, and even conducting environmental investigation by experts for difficult cases is helpful for diagnosis.
4. Lung function indicates ventilation disturbance, serum-specific IgG is positive, lymphocyte count in bronchoalveolar lavage fluid (BALF) is increased, and inflammatory cell infiltration, multinucleated giant cells, non-necrotizing granuloma, and fibrous tissue hyperplasia are found in fiberoptic bronchoscopy and lung biopsy.
5. Natural provocation test shows positive results.

21.5 Differential Diagnosis

The imaging manifestations of hypersensitivity pneumonitis are similar to those of bronchitis, interstitial pneumonia, pulmonary tuberculosis, and idiopathic pulmonary interstitial fibrosis. If the occurrence of the lesions is related to a certain working and living environment, the lesions are likely to occur in the middle and upper lungs, with ground-glass opacities and lobular nodules, which suggests hypersensitivity pneumonitis. Idiopathic pulmonary fibrosis is most serious at the base of the lung, but central lobular nodules are not common, and reticular opacities and honeycomb shadow are relatively common.

21.6 Research Status and Progress

The imaging manifestations of hypersensitivity pneumonitis are complex but lack specificity. At present, studies mainly focus on some relatively specific signs, such as mosaic attenuation and "air retention" sign [17, 18], for better differential diagnosis and prognosis estimation. Based on these signs, relevant models are established by using statistical data methods, thereby guiding clinical practice by analyzing imaging manifestations [19].

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