

FOCUS ON THE HOME ENVIRONMENT: THREE PATIENTS WITH HYPERSENSITIVITY PNEUMONITIS IN ONE FAMILY

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ABSTRACT

Repeated inhalation of organic antigens is a main cause of hypersensitivity pneumonitis (HP). We reported three patients with mould-induced HP from one family residing in a wet environment. Measures to minimise antigen exposure resulted in regression of HP. This highlights the association between HP and domestic environment, and emphasises the importance of environmental control in HP treatment.

Hypersensitivity pneumonitis (HP), also known as extrinsic allergic alveolitis (EAA), is a diffuse inflammatory lung disease caused by repeated inhalation of various antigens derived from fungi, bacteria, and animal and plant proteins or reactive inorganic compounds in sensitised individuals.¹ Fungi represent a large source of antigens capable of causing HP, which is often related to the patient's occupation or domestic environment. Three patients diagnosed with HP from one family, residing in a wet environment, were reported here.

CASE REPORT

PATIENT 1

A 14 year old boy was admitted to Shanghai Pulmonary Hospital because of chest tightness, shortness of breath, and fever. The patient had experienced these symptoms for one month before seeking medical help. The patient had worsening symptoms while he was at home but improved outside. The environmental history revealed no contacts with pets or birds. The family had lived in the same house for several years. There was some mould covering the walls and floors, due to roof leaking, in heavy rain. The patient had consulted many doctors and antibiotics were prescribed but there was no improvement.

His systemic examinations were unremarkable. The chest radiograph indicated bilateral micronodules with ground-glass opacity and areas of hyperlucency (Figure 1 a-d).

Pulmonary function tests revealed a forced vital capacity (FVC) of 52%, FEV1 of 60%, FEV1/FVC of 85%, and diffusion capacity for carbon monoxide (TLCO) of 65% of the adjusted reference values, respectively. Arterial blood gas showed a PH of 7.48, carbon dioxide tension of 3.95 kPa (29.6 mmHg), and oxygen tension of 6.1 kPa (46 mmHg). The erythrocyte sedimentation rate was 50 mm/h. The total immunoglobulin (Ig) E was 1160 ku/l.

We initiated treatment with prednisolone 0.5 mg/kg body weight/day for the boy and advised the family to move out of the house temporarily and clean the house completely. Four weeks later the steroid dose was tapered and stopped after an additional eight weeks. The patient's clinical condition and subsequent chest radiographs and lung function tests showed gradual improvement (Figure 1 e-h).

PATIENT 2

A 39-year-old woman, the boy's mother, was admitted to Shanghai Pulmonary Hospital because of a dry cough and wheezing. The patient had experienced these symptoms for one month before seeking medical help. The physical examination was unremarkable except for crackles over the left lung base. High-resolution chest CT demonstrated ground-glass opacity and fine nodules with a mosaic pattern (Figure 2 a-c).

The haemoglobin level was 13.0 g/dl, and white blood cell count, serum chemistry were all within the reference values. The total IgE was 985 ku/l.

Pulmonary function tests were also done according to published ATS/ERS guidelines. Pulmonary function tests revealed a forced vital capacity of 54%, FEV1 of 61%, FEV1/FVC of 89%, and TLCO of 69% of the adjusted reference values, respectively.

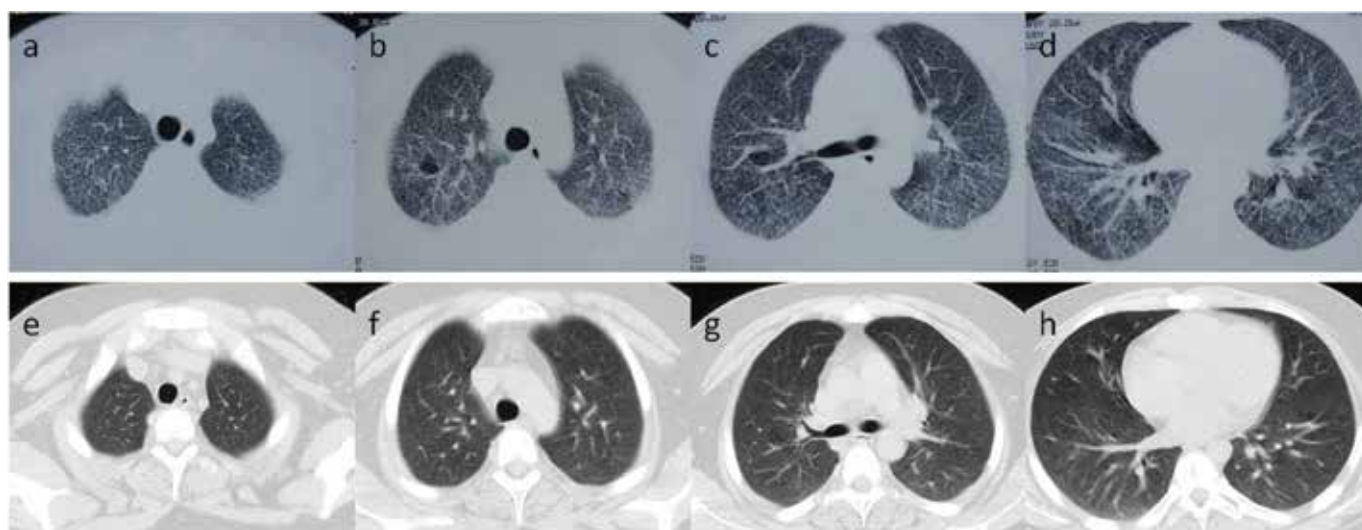


Figure 1. Chest CT demonstrating bilateral micronodules with ground-glass opacity and areas of hyperlucency in patient 1 (a-d). After 4-week prednisolone treatment and antigen avoidance, CT scan showing radiologic normality (e-f).

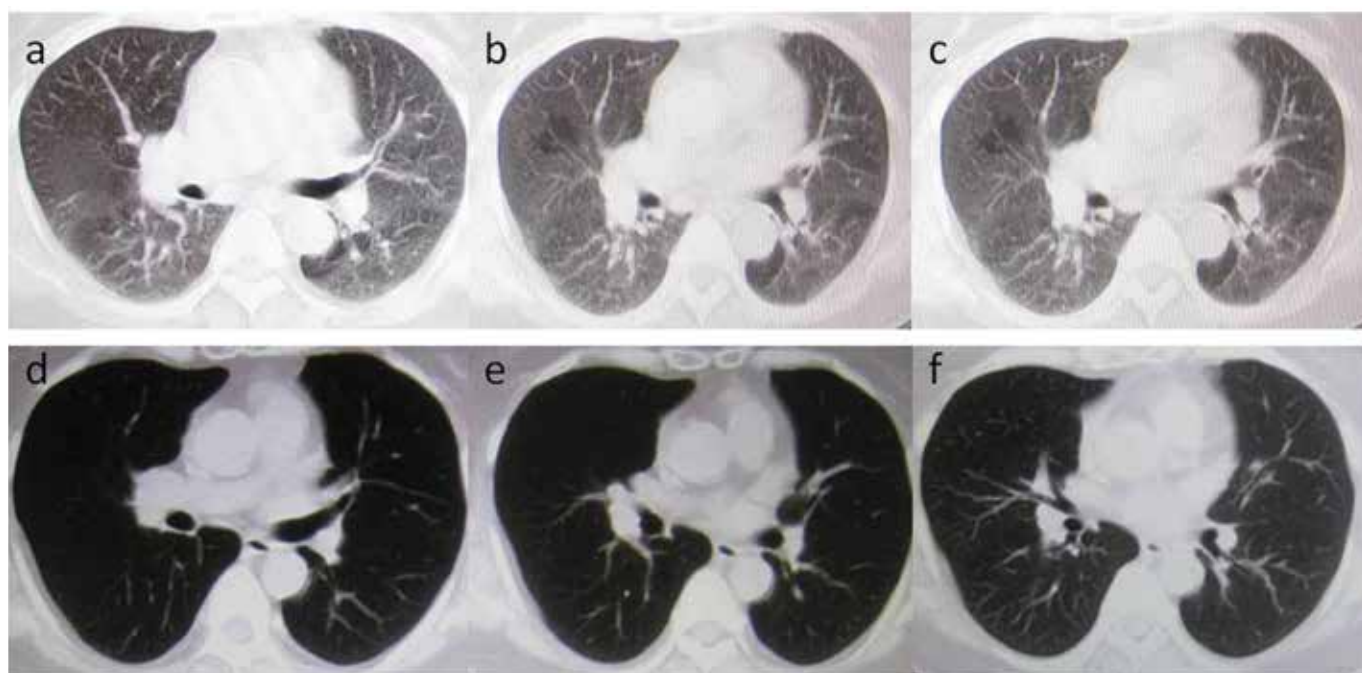


Figure 2. Chest CT demonstrating ground-glass opacity with mosaic pattern in patient 2 (a-c), and radiologic normality after 1-month antigen avoidance without any medications (d-f).

Arterial blood gas showed a PH of 7.43, carbon dioxide tension of 3.47 kPa (26 mmHg), and oxygen tension of 10.67 kPa (80 mmHg). Broncho-alveolar lavage (BAL) was performed through the lingual bronchus (5×20 ml of saline, recovery rate 50%). The BAL fluid yielded a proportion of 80% lymphocytes with a CD4/CD8-ratio of 0.51. The transbronchial lung biopsy (TBLB) and histological analysis showed an infiltration of alveolar spaces and interstitium with lymphocytes and foamy macrophages, which is

consistent with a diagnosis of hypersensitivity pneumonitis (Figure 3).

She moved to another place with her family without any medication. At the 1-month follow up, symptom improvement was noted with relief of dry cough and wheezing. The radiological finding was normal (Figure 2 d-f).

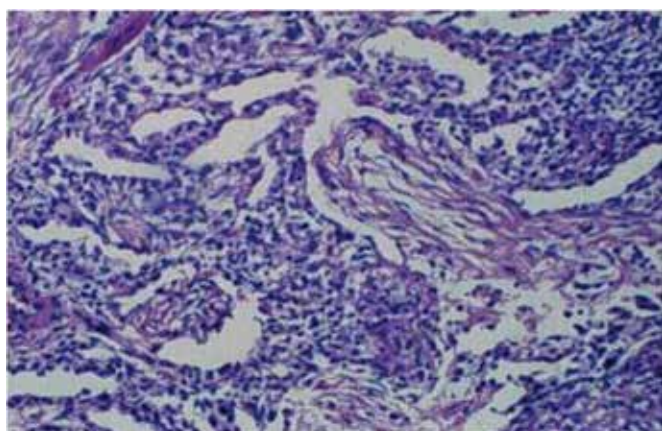


Figure 3. Transbronchial lung biopsy (TBLB) and histological analysis showing an infiltration of alveolar spaces and interstitium with lymphocytes and foamy macrophages.

PATIENT 3

A 50-year-old man, the boy's father, presented with cough and chest tightness. The patient had experienced these symptoms for one month before seeking medical help. He had no suggestive history of atopy. No pets were kept in his house. He had a history of smoking a 10 pack of cigarettes for years but had stopped for 1 year. He was initially treated for chronic obstructive pulmonary disease (COPD) with

albuterol and corticosteroid inhalers with no improvement. At the time of hospital admission, the physical examination revealed no obvious respiratory distress except for bibasilar fine crackles. High-resolution chest CT showed ground-glass opacity (Figure 4 a-c).

Pulmonary function tests revealed a vital forced capacity of 60%, FEV1 of 63.3%, FEV1/FVC 61.7%, and TLC0 of 61% of the adjusted reference values, respectively. Complete blood count with differential analysis, serum electrolytes, liver function tests, urinalysis, erythrocyte sedimentation rate, antinuclear antibody and rheumatoid factor were all normal. The sputum culture result was negative.

BAL was performed through the lingual bronchus (5×20 ml of saline, recovery rate 60%). The BAL fluid yielded a proportion of 83% lymphocytes with a CD4/CD8-ratio of 0.55.

He moved to another place with his family without any medication. At the 1-month follow up, symptom improvement was noted with relief of dry cough and chest tightness. Radiological improvement also occurred (Figure 4 d-f).

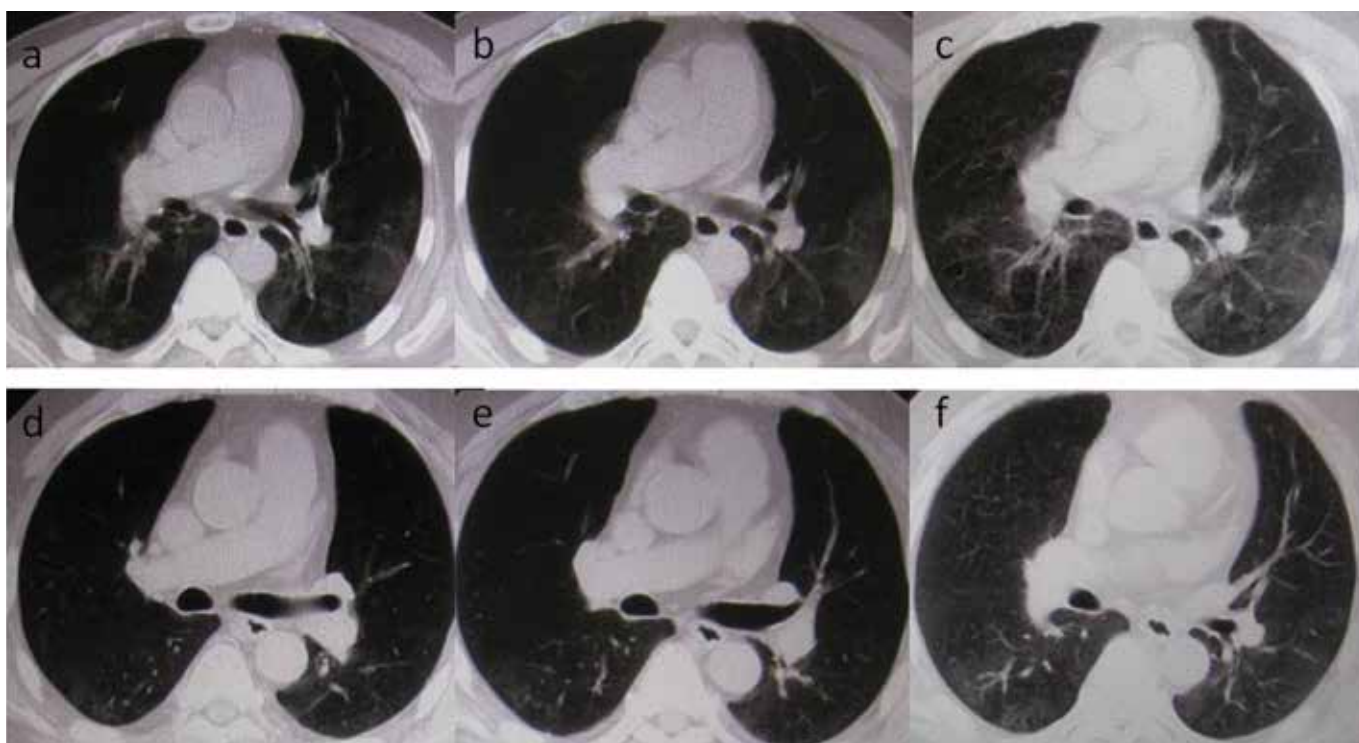


Figure 4. Compared with baseline (a-c), chest CT showing radiologic improvement in patient 3 after 1-month antigen avoidance without any medications (d-f).

ANALYSIS OF THE ENVIRONMENT FUNGUS

Samples from the air and floors of the house were collected using sterile 100 ml vessels. Sample aliquots (undiluted; 1:10; 1:100; 1:1000; 3 X 100×l each) were plated onto malt extract agar (25°C) and DG 18 agar (25 and 37°C). The number of colony forming units (CFU) was counted after 48 hours at 37°C and 5-10 days at 25°C and fungal CFUs were differentiated to species level by light microscopy according to standard methods and keys.² The samples revealed *Aspergillus fumigatus* as the dominant fungal micro-organism (104 CFU/ml) and *Candida* species at lower concentration (Figure 5).

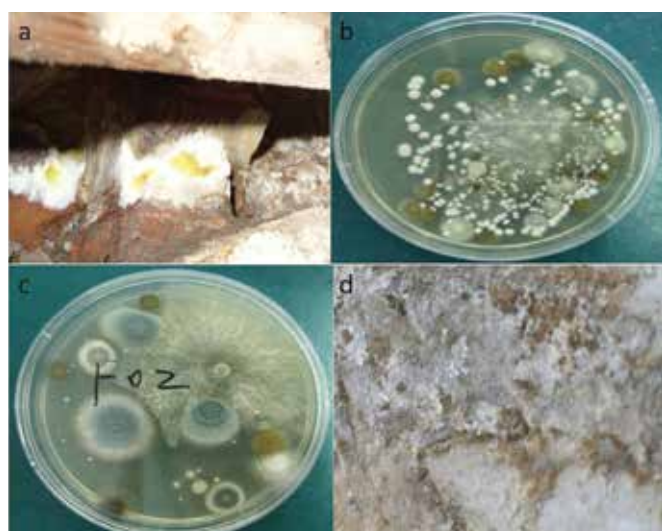


Figure 5. The samples revealed *Aspergillus fumigatus* as the dominant fungal micro-organism (104 CFU/ml) and *Candida* at lower concentration.

Screening for precipitating antibody in three patients' serum was performed. The investigation was based on the usual solid phase peroxidase IgG enzyme-linked immunosorbent assay using Nunc Maxisorb microplate, as described by Tijssen. Precipitating antibodies could be detected against *Aspergillus fumigatus*.

The diagnosis of HP relied on the typical clinical symptoms and signs developed in an appropriate setting for HP, demonstrating fine nodular, ground-glass opacity and reticular density on chest radiographs, serum precipitating antibodies against offending antigens with proven exposure to this antigen, a lymphocytic alveolitis on BAL, and a corresponding reaction on the lung biopsy, thus fulfilling the major diagnostic criteria of HP.

DISCUSSION

In this report we described three patients with HP from one family associated with fungal contamination in their home environment. HP is often associated with exposure to antigens in the home environment and the most significant diagnostic tool is a detailed environmental exposure history taking and inspection. Samples from the air and floors of the house revealed *Aspergillus fumigatus* as the dominant fungal micro-organism. Based on a thorough investigation, the domestic environment contaminated with *Aspergillus fumigatus* was identified as the most probable source of the HP in these cases.

HP is caused by a wide variety of antigens. These include bacteria, organic materials, fungal spores and chemicals.³⁻⁶ The exposure to these antigens occurs in various settings including occupational, recreational and environmental area. Although many allergens in the environment can trigger HP, house dust is the main culprit in indoor allergies. House dust is an airborne mixture that might contain fine particles of soil and plant material from indoors or outdoors, particles of human and animal skin (dander) and hair, fabric fibres, mould spores, dust mites, fragments of insects that have died and their waste, food particles, and other debris. Moulds are fungi that can be found both outdoors and indoors. There are many types of mould; all need moisture to grow. They can be found in damp areas such as basements or bathrooms, as well as in grass or mulch. They grow best in warm, damp and humid conditions. If you have damp or wet spots in your house, you will probably get mould. However, only a minority of subjects exposed to the antigens develop EAA, therefore individual susceptibility is important.⁴ Environmental and host factors are responsible for the pathogenesis of HP. Inhaling or touching mould or mould spores may cause allergic reactions in sensitive individuals. It is important to prevent HP by ventilating moist areas in the home and avoiding activities that trigger symptoms, such as raking leaves.

Patients with severe symptoms should be considered for a trial of steroid therapy to suppress the active immune response. A randomised controlled trial in acute Farmer's Lung found that prednisolone improved lung function compared with the control group, but there was no difference in the long-term outcome between the two groups.⁷ The effects of corticosteroids might not always be entirely beneficial in HP. Antigen avoidance should be the main focus of therapy. Each patient's treatment needs to be individualised. The effectiveness of steroid trial and antigen avoidance measures can be guided by clinical symptoms,

chest radiographs, lung function tests and circulating antibody levels.

In the chronic form of the disease, subsequent antigen avoidance may not reverse the disease and some patients continue to have progressive deterioration of lung function despite avoiding antigens and undergoing treatment. These changes are likely to be irreversible and lead to respiratory failure, cor pulmonale and ultimately death. Lung transplantation may be the last resort in patients with progressive disease that are unresponsive to medical therapy.

CONCLUSION

This report highlights the association between HP and the domestic environment, and alerts physicians in the diagnosis of HP in antigen-exposed individuals. Emphasis on environmental control is the cornerstone of HP treatment. Timely diagnosis of HP and avoidance of causative antigens may prevent progression impairment.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review from the Editor-in-Chief of this journal.

COMPETING INTERESTS

The authors declare no conflict of interest.

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