

Dear Editor

Non Occupational Chronic Hypersensitivity Pneumonitis due to *Aspergillus fumigatus* on Leaky Walls

Aspergillus is a common fungus that causes variety of human diseases, depending on the host response. Hypersensitivity pneumonitis (HP) caused by *Aspergillus* is usually seen in an occupational setting, and case of farmer's lung caused by *Aspergillus fumigatus* have also been reported.¹⁻³ It is known that environmental *A. fumigatus* exposure rarely causes home-related chronic HP. There are few case reports of nonoccupational chronic HP caused by *A. fumigatus*, the diagnosis of which was confirmed by a provocation test.

A 74-year-old Japanese smoker presented with dry cough dating back 15 years. He lived in a 25-year-old reinforced concrete house. For 20 years, the house leaked when it rained, and the wallpapers of the hallway and bedroom became moldy.

He first visited our hospital in November 2009, and high-resolution computed tomography (HRCT) demonstrated bilateral fibrotic shadows in the upper lobes but with poorly defined ground-glass opacity (GGO). Laboratory examinations at that time showed a surfactant protein D (SP-D) level of 167 ng/ml and a KL-6 level of 783 U/ml. He has been seen in patients with idiopathic pulmonary fibrosis (IPF).

He removed the moldy wallpaper in the rainy season, and during the next two months his shortness of breath and dry cough worsened. Laboratory examinations in October 2010 showed an SP-D level of 347 ng/ml and a KL-6 level of 2390 U/ml. Chest x-ray shows diffuse consolidation with small nodules in the bilateral lungs. HRCT showed GGO and fibrosis in

the mid-to-lower lobes (Fig. 1).

Spirometry revealed a forced vital capacity (FVC) 79.1% of predicted, a forced expiratory volume in 1 second (FEV₁) 92.9% of predicted, a FEV₁/FVC of 79.3%, and a diffusion capacity (DLco) 70.9% of predicted. The bronchoalveolar lavage fluid (BALF) revealed lymphocytosis (62%) with a CD4⁺/CD8⁺ ratio of 6.01. A transbronchial lung biopsy showed lymphocytic alveolitis.

Serum-precipitating antibodies to *Aspergillus fumigatus* and *Aspergillus flavus* were positive among 12 fungal species. The precipitate line of *A. flavus* overlapped with that of *A. fumigatus*, which indicated the cross reactivity of *A. flavus* with *A. fumigatus*. Late-phase skin test reaction for *A. fumigatus* was positive. An allergen-specific lymphocyte stimulation test for the *A. fumigatus* antigen was performed using peripheral blood mononuclear cells. The stimulation index was 11.5. The IFN- γ , IL-5, and IL-13 concentrations in the culture supernatants were 725.7, 643.5, and 12108.6 pg/ml, respectively, and in the absence of the antigen, their concentrations were 15.0, 1.3, and 5.8 pg/ml, respectively.

Samples from the wallpaper and bedroom-floor dust revealed contamination by *A. fumigatus*. Cultures of the indoor air obtained by volumetric air sampler in the house grew mainly *A. versicolor* and *Penicillium*. *Cladosporium* was most frequently isolated from air samples collected from his house. Environmental sampling was performed using a volumetric air sampler and airborne particles were collected onto dichloran glycerol (DG-18) media.⁴

The diagnosis was definitively confirmed by performing a specific bronchial provocation test for *A. fumigatus*. He inhaled 1 ml of an *A. fumigatus* antigen solutions (10 mg/ml) through a nebulizer for 2 minutes. Six hours after the challenge, the patient developed fever, hypoxemia (oxygen arterial pressure de-

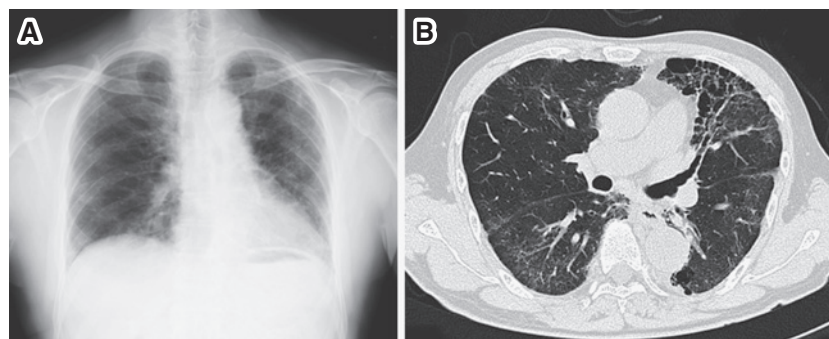


Fig. 1 Chest x-ray (A) and Transverse thin-section CT scans at level of distal trachea (B) at symptoms exacerbation. Chest x-ray (A) shows diffuse consolidation with small nodules in the bilateral lungs. HRCT (B) shows bilateral patchy areas of GGO and bronchiectases due to interstitial fibrosis.

creased from 76.3 to 64.7 Torr) and elevation of alveolar-arterial oxygen partial pressure (PA-a, O₂: from 19.3 to 31.8 Torr). Twenty-four hours after the challenge, cough and crepitant rales worsened. Forty-eight hours after the provocation, C-reactive proteins level increased from 0.8 to 2.08 mg/dl, and functional respiratory deterioration occurred (FEV1 decreased from 2.07 to 1.84 L, FVC from 2.64 to 2.48 L). When he inhaled 1 ml of a *Cladosporium* antigen solutions (10 mg/ml), no specific changes were induced.^{3,5}

The final diagnosis was chronic HP caused by *A. fumigatus* growing in his house because of leaky walls. Four months of corticosteroid therapy and removal of the antigen from his house led to partial improvement of his symptoms, but night cough remained. He had been exposed to the antigen for a long time, which may have resulted in irreversible fibrosis.

This case report is valuable because it confirmed the diagnosis of chronic HP caused by environmental *A. fumigatus* exposure by an inhalation test. The diagnosis of chronic HP is difficult, since the onset may be insidious and some of chronic HP patients showed no response to inhalation challenge.⁶ There may be many undiagnosed cases of idiopathic pulmonary fibrosis caused by environmental fungi, because it is difficult to prove the relationship between exposure to fungi and the pathogenesis of the disease particularly in chronic cases. We should consider *A. fumigatus* as more prevalent cause of chronic HP in patients living in moldy houses.

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