

Hypersensitivity pneumonitis by *Fusarium vasinfectum* in a home environment

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Clinical Implication

- To our knowledge, this is the first report of hypersensitivity pneumonitis caused by *Fusarium vasinfectum*, a large nonrespirable mold spore, in a home environment.

TO THE EDITOR:

Hypersensitivity pneumonitis (HP) is a complex inflammatory response typical to an organic antigen. HP requires a combination of (1) an environment that provides the correct type and amount of exposure to a potential antigen, and (2) a corresponding robust lymphocytic response from the host. This disease may prove challenging to diagnose because the clinical symptoms, such as cough, fever, and dyspnea, are nonspecific, and not all cases present with other classic diagnostic criteria.¹ Precipitins to the causative antigen, noncaseating granulomas on lung biopsy specimens, interstitial opacities on radiologic studies, and a low CD4-CD8 ratio on bronchoalveolar lavage may not always be demonstrated. The environmental history may not suggest a possible cause. Disease activity may lessen the possibility of environmental challenges to determine the causative antigen because the more chronic or indolent forms are unlikely to respond within a workable time frame.

Most reports of HP have focused on antigens derived from feathers and droppings of birds, thermophilic actinomycetes exposure of farmers, and other antigenic materials that are respirable to the alveolar level. Even though this is considered to be a rare disease, the unique clinical setting in which the disease develops (eg, mushroom farmers, metal workers, poultry workers) can assist the clinician in making the correct diagnosis. The more ubiquitous molds and their roles in HP in a non-workplace environment need to be emphasized.

A 69-year-old woman, lifelong nonsmoker and with an unremarkable respiratory history, was evaluated with a 1-year history of recurrent episodes of difficult-to-treat respiratory symptoms. Her episodes consisted of fevers up to 101°F, chest pressure, and a productive cough of white-to-green sputum. Results of laboratory data showed white blood cell counts of up to 21,000/mm³ (350/mm³-10,500/mm³) and erythrocyte sedimentation rates of up to 99 mm/h. She had a total of 5 episodes in 1 year before she was evaluated by a pulmonary specialist. Chest radiographs done over that year showed progressive reticulonodular densities with multilobar pneumonia. Pulmonary function tests showed a severe restrictive pattern with a severe reduction in lung carbon monoxide diffusing capacity. A trans-bronchial lung biopsy specimen showed evidence of noncaseating granulomas, with negative Gram, silver, periodic acid-Schiff, and acid-fast stains. Sputum bacterial cultures revealed normal respiratory flora. A precipitin panel to molds was positive for *Fusarium vasinfectum*. An environmental investigation by one of

the authors (R.L.J.) revealed a heavily cluttered, dank home with large numbers of cardboard boxes filled with various items. There was no significant odor detected. There was carpet throughout the house, 2 window air-conditioning units, and central heat. By using a Delmhorst moisture meter, high levels of moisture were found in the wall under the master bedroom air-conditioning unit as well as in the floor underneath the carpet. Gravity air cultures as well as cultures by using an Anderson sampler at 2 and 10 minutes were obtained.² All the cultures had a strong predominance of *Fusarium vasinfectum* identified by a medical mycologist. The recommendation was then made to make the appropriate repairs at home or move to a different environment. She did not have any significant occupational exposure.

Cases of lower respiratory disease provoked by *Fusarium vasinfectum* are rare. Two cases of allergic bronchopulmonary mycosis have been reported.^{3,4} Two publications identified serum precipitins in patients with HP; however, in neither article was there confirmation that *Fusarium vasinfectum* was the causative antigen.^{5,6} Our patient had a continuous daily exposure to high levels of mold within her home. She met the major criteria of a consistent clinical medical history, consistent pulmonary functions, computed tomography of the chest that showed migrating opacities, positive serum precipitins to the antigen cultured in heavy concentration from her home, and a home investigation that confirmed a massive contamination by *Fusarium vasinfectum*. Normal eosinophil counts, total IgE of 91 IU/mL, and a lack of IgE to molds ruled out other possibilities, for example, allergic bronchopulmonary mycosis. These factors make a very strong argument that *Fusarium vasinfectum* exposure led to HP, without doing a potentially dangerous direct challenge in this highly compromised patient. A recent report of HP due to *Fusarium napiforme* exposure at home, confirmed by an assessment of the home environment and with confirmatory laboratory data, shows a similar presentation to ours.⁷

A reason why *Fusarium* does not commonly cause HP may be the size of the spore. The spindle-shaped *Fusarium* spores can measure up to 40 µm in length,⁸ which is larger than particles that can reach the alveoli. Particles that are smaller than 5 µm, such as *Aspergillus* and the thermophilic spores, are more commonly causative. The pathogenesis of HP hinges on the development of a robust Th1 response to small antigens that reach the terminal alveoli, which then leads to fibroblast proliferation, extracellular matrix deposition, and possible granuloma formation.⁹ There are limited data to explain how large particles such as *Fusarium* spores reach the alveoli. Studies that look at pollens that are too large for the airways have shown that allergenic material released by pollens can bind to small particles that can reach deeper in the pulmonary tree.¹⁰ In a similar fashion, mold antigens could reach deeper in the bronchial tree as opposed to the whole spore. For example, *Alternaria* spores will release most of their allergens into their surroundings when they are germinating.¹¹ More studies are needed to better understand this process.

HP is seen primarily as an occupational disease¹²; however, many patients are not working in possible causative environments. Hanak et al¹³ described 85 consecutive patients to assess the spectrum of cause. In this study, the cause was identified in 75% of patients (avian antigens [34%], *Mycobacterium avium* in

hot tubs [21%], farmer's lung [11%], and household mold exposure [9%]) with 25% of the patients retired or for whom no occupational cause could be implicated. Similarly, Jacobs et al⁶ reported that the focus of the causative environment should be on the home after initial queries on the workplace. In conclusion, we report a case of HP caused by an unlikely antigen in an unlikely environment, which underscores the need to broaden the discussion concerning the causes and the mode of exposure when evaluating HP.

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