
Case report

Hypersensitivity pneumonitis secondary to residential exposure to *Aureobasidium pullulans* in 2 siblings

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Background: Hypersensitivity pneumonitis (HP) is an immune-mediated hypersensitivity reaction to a variety of inhaled particles that may lead to acute, subacute, or chronic interstitial pneumonitis and possibly end-stage lung disease. Avian antigens most commonly cause HP in children, but fungi have also been implicated.

Objective: To describe a 15-year-old girl and her 6-year-old brother who developed HP from residential exposure to *Aureobasidium pullulans*.

Methods: Allergy skin testing, serum precipitating antibodies, pulmonary function testing, chest radiography, chest computed tomography, bronchoalveolar lavage, and a home survey for possible causative antigens were performed.

Results: Both patients lived on a horse farm and had fatigue, weight loss, cough, and dyspnea. The siblings had restrictive patterns on pulmonary function tests, with decreased diffusion capacity of carbon monoxide, ground-glass opacities on high-resolution chest computed tomography, and serum precipitins to *A pullulans*. Bronchoalveolar lavage in the girl demonstrated lymphocytosis, with a preponderance of CD8⁺ T cells and natural killer cells. Symptoms improved after the children vacated the home and recurred on repeated exposure in both patients. Home evaluation revealed extensive mold contamination, with *A pullulans* counts of 659, 329, and 71 CFU/m³ in the boy's bedroom, the girl's bedroom, and outdoors, respectively.

Conclusions: The diagnosis of HP in these siblings is supported by the clinical history, the diagnostic findings, and the recurrence of symptoms on repeated exposure. These cases represent the second report of HP resulting from nonoccupational exposure to *A pullulans* in North America and the first report in children.

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INTRODUCTION

Hypersensitivity pneumonitis (HP) is an immune-mediated hypersensitivity reaction to a variety of inhaled particles that may lead to acute, subacute, or chronic interstitial pneumonitis and possibly end-stage lung disease. Most adult cases are associated with occupational antigen exposure.¹ HP due to *Aureobasidium pullulans*, or sequoiosis, was first described by Cohen et al² after exposure to moldy redwood dust. Since then HP secondary to *A pullulans* has been described in adults with occupational exposure to moldy water from heating/

ventilation/air-conditioning systems or home saunas.^{3–6} A recent case of HP in a woman was attributed to exposure to *A pullulans* in a water-damaged home.⁷ Herein we describe the first cases of childhood HP secondary to *A pullulans* from home exposure in 2 siblings.

Report of Cases

A 15-year-old girl with no significant medical history presented to the emergency department (ED) with a 2-month history of night sweats, chills, cough, dyspnea, anorexia, and a 23-lb weight loss. She had been treated with antibiotics for recurrent respiratory tract infections in the 3 months preceding admission. The only difference in her daily routine during this period was that she was spending more time at home because the school year had ended.

The patient lived on a horse farm with several animals, including outdoor chickens and a peacock. The family had 3 dogs, 1 guinea pig, and 1 hamster that stayed indoors. No agricultural activities occurred on the farm. The patient's father noted possible mold in the basement where an addition was being built. Family history was negative for allergic, rheumatologic, or pulmonary disorders. There was no history of tobacco use or illegal drug use.

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On admission she required 7 L of oxygen via a face mask to maintain oxygen saturations of 93%. Physical examination revealed a temperature of 38.3°C, a respiratory rate of 30/min, and bibasilar crackles. Findings from routine laboratory work, including complete and differential blood cell counts, serum electrolytes, urinalysis, urine culture, and a B-natriuretic peptide, were negative. Serum immunoglobulins revealed an elevated IgG level, with normal IgA and IgM levels. Rheumatoid factor, antinuclear antibody, antineutrophil cytoplasmic antibody, anti-SSA, and anti-SSB titers were negative.

Chest radiography revealed bilateral reticulonodular infiltrates, and computed tomography (CT) of the chest revealed bilateral ground-glass opacities (Fig 1). Echocardiographic findings were normal. Pulmonary function testing (PFT) revealed a restrictive defect, decreased diffusion capacity of carbon monoxide (DLCO), and significant reversibility after bronchodilator therapy (Table 1). The patient underwent bronchoalveolar lavage (BAL) using a saline wash through a bronchoscope. Flow cytometry of the BAL fluid (BALF) revealed lymphocytosis, with 60% CD8⁺ T cells, 12% natural killer cells, and a CD4⁺/CD8⁺ ratio of 0.24. All cultures of BALF were negative. After 3 days of inpatient observation and antibiotic therapy for a possible community-acquired pneumonia, she improved remarkably, and supplemental oxygen therapy was discontinued.

The 6-year-old brother of this patient presented to the ED, approximately 3 weeks after his sister's discharge, with a 1-month history of cough, dyspnea, fatigue, anorexia, and a 5-lb weight loss. He had no significant medical history. Social, family, and environmental histories were the same as those for his sister. On presentation he required 2 L of oxygen via nasal cannula to maintain oxygen saturations of 93%, and he experienced oxygen desaturations to 85% with walking in the ED. Physical examination revealed tachypnea and bibasilar crackles. Complete and differential blood cell counts and serum electrolyte levels were normal. Chest radiography revealed bilateral infiltrates, and CT of the chest revealed ground-glass opacities and micronodules. PFT demonstrated

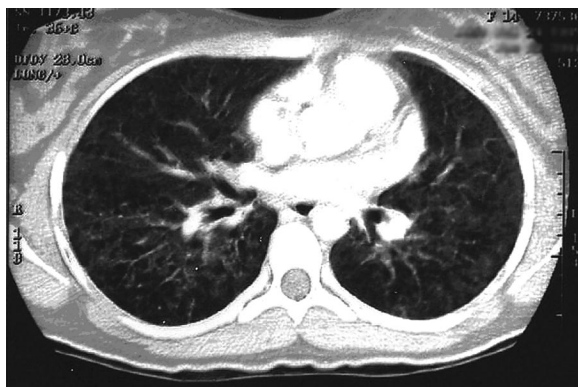


Figure 1. Chest computed tomographic scan in the 15-year-old girl demonstrating ground-glass opacities.

Table 1. Pulmonary Function Test Results in the 15-Year-Old Girl

	Initial PFTs ^a		% Change	Repeated PFTs (3 mo), Pre-BD ^a
	Pre-BD	Post-BD		
FVC	69	80	17	95
FEV ₁	60	74	24	93
FEF _{25%-75%}	67	103	54	119
FEV ₁ /FVC	0.83	0.88	NA	0.88
VC	71	80	NA	98
TLC	86	82	NA	99
DLCO	63	NA	NA	85

Abbreviations: BD, bronchodilator; DLCO, diffusion capacity of carbon monoxide; FEF_{25%-75%}, forced expiratory flow during the middle half of the FVC; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; NA, not available; PFTs, pulmonary function tests; TLC, total lung capacity; VC, vital capacity.

^a Data are given as percentage of predicted except for FEV₁/FVC, which is given as a ratio.

a restrictive defect with a decreased DLCO but was limited by the patient's age and difficulty with the forced vital capacity maneuver.

Both patients had negative results of commercial peripheral blood HP panels testing *Thermoactinomyces vulgaris*, *Micropolyspora faeni*, pigeon serum, *Saccoromonospora viridis*, *Aspergillus fumigatus*, *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, and *Thermoactinomyces candidus*. Serum precipitating antibodies were then performed to a variety of antigens, including *Aspergillus fumigatus*, *A. pullulans*, and avian antigens that were extracted from chicken and peacock droppings from the farm. A positive reaction was found to *A. pullulans* in both children. Both patients had recurrence of symptoms within 4 hours of revisiting the home.

Given the consistent clinical findings for a diagnosis of HP and positive precipitating antibodies to *A. pullulans* but lack of a known inciting exposure, a home evaluation was performed. An addition was being added to the home, with construction of a basement that was covered with a tarp and wood planks (Fig 2), with nothing else preventing exposure of the basement to the outdoor elements. A small portion of the basement was under the home and had standing water and extensive mold contamination, presumably due to outdoor rainfall (Fig 3). A pungent, moldy odor was immediately perceptible on entering the home. Mold contamination was obvious on the walls of the kitchen, the bathroom, and the sister's bedroom. Moldy horse saddles were stacked in the foyer. Burkard and Anderson samplers were placed and surface sampling was performed inside the home. Mold counts from the Anderson sampler are listed in Table 2. All surface and air samples collected were cultured on cellulose (Rose Bengal) agar to identify cellulolytic fungi. Fungal contamination was noted throughout the home, with *Aureobasidium* levels of 659.2, 329.6, and 70.63 CFU/m³ in the boy's bedroom, girl's bedroom, and outdoors, respectively.



Figure 2. Outdoor view of the home and basement with overlying tarp and wood.



Figure 3. Basement with standing water and debris.

Both patients required a corticosteroid taper for 2 to 3 months and removal from the offending environment. Close follow-up was necessary because they commonly experienced minor deterioration that necessitated an increase in or a continuance of the corticosteroid dose. Frequent PFT was performed to monitor response to therapy. Although both patients regained normal pulmonary function, they both developed asthma after the HP episode. Both children continued to demonstrate reversibility after bronchodilator therapy and cough and wheeze 1 year after diagnosis of HP despite resolution of radiographic abnormalities. Allergy skin test results were negative to the inciting agent, *A pullulans*, in both children. Both patients required treatment with inhaled corticosteroids and long-acting β -agonists for continued control of asthmatic symptoms 1 year after initial diagnosis of HP.

DISCUSSION

HP is an underrecognized form of interstitial lung disease in children and is typically caused by avian or fungal antigens in the home.⁸ Mold antigens reported to cause HP in children include those from *Aspergillus*, *Penicillium*, *M faeni*, *Trichosporon cutaneum*, *Epicoccum nigrum*, and *Fusarium napi-*

forme.⁸⁻¹⁴ Identification of the offending antigen and source of exposure is important because continued exposure can lead to irreversible pulmonary fibrosis and chronic lung disease. Because HP is due to complex associations between the intensity and duration of antigen exposure, genetic predisposition, and host susceptibility factors, it can have varied presentations.¹⁵ Although high levels of antigen exposure are typically necessary for the development of HP, only 5% to 15% of patients with such a history develop clinical disease.^{1,8,16,17}

The 6 major diagnostic criteria are (1) a history of symptoms compatible with HP, (2) evidence of exposure to the offending antigen by history or through detection of antibody in serum or BALF, (3) radiographic changes consistent with HP, (4) BAL lymphocytosis, (5) histologic changes consistent with HP on lung biopsy, and (6) a positive natural challenge that produces symptoms or objective abnormalities on reexposure to the offending environment or through controlled inhalational challenge.¹⁸ The minor criteria are bibasilar rales, decreased DLCO, and arterial hypoxemia at rest or with exertion. The diagnosis is confirmed when 4 major and 2 minor criteria are met. Both patients satisfied these criteria.

Note that neither patient reacted to commercial HP panels. Detection of precipitating antibodies is a necessary step in the workup of HP. Although 40% to 50% of individuals exposed to a potential inciting antigen will have positive precipitins without disease, the presence of precipitins documents sufficient exposure to generate a humoral immune response.¹⁹ Negative precipitins should not be used to reject the HP diagnosis because false-negative precipitins may result from improper quality controls, insensitive techniques, use of wrong antigens, or use of underconcentrated serum.²⁰ Some patients may have a weak antibody response that cannot be detected with serum precipitins, and some with chronic HP who have been removed from their antigen source may have waning of their antibody response across time.¹⁵⁻²⁰

The development of asthma after a diagnosis of HP has been described in patients with farmer's lung, in HP caused by diisocyanates, and after summer-type HP.²¹⁻²⁴ Allergy skin test results were positive to the inciting antigen in some of these cases.^{23,24} In the present cases, however, allergy skin test results were negative to the inciting agent, *A pullulans*.

Recently it has been suggested that exposure to specific indoor fungal spores may be an extremely unlikely cause of HP, except in highly unusual circumstances, such as with workplace exposure.²⁵ The present cases indicate that HP can occur in susceptible individuals with a significant exposure burden in the residential setting. Also, HP in children is more commonly associated with household exposures, as previously noted.⁸ We stress the diagnostic benefit of a home visit. In these 2 cases mold exposure was not thought by the family to be a potential cause of the patients' symptoms. Whereas this family did not notice the degree of mold contamination in the house, it was readily evident to us.

We suggest that when entertaining the diagnosis of HP an inquiry into home exposures is necessary but may not be

Table 2. Mold Counts by Location From the Environmental Evaluation^a

Mold species	Outdoor	Boy's BR ^b	Girl's BR ^b	Rear BR ^b	Hall ^c	Living room ^c	Bath ^c	Saddle ^c
<i>Aureobasidium</i>	70.63	659.20	329.60	0	211.89	47.09	0	164.80
<i>Alternaria</i>	164.80	23.54	0	47.08	0	0	0	0
<i>Aspergillus</i>	0	94.17	117.72	0	141.25	329.61	1,012.35	0
<i>Chrysosporium</i>	0	117.72	141.26	70.63	306.06	70.63	0	117.72
<i>Cladosporium</i>	3,837.51	1,577.38	1,271.32	353.15	353.15	753.38	894.63	1,294.87
<i>Epicoccum</i>	117.72	23.54	0	0	23.54	0	0	306.06
<i>Fusarium</i>	235.43	141.26	117.72	0	47.09	23.54	70.63	141.26
<i>Nigrospora</i>	0	0	0	0	0	47.09	0	0
Nonsporulating	0	0	0	0	23.54	0	0	0
<i>Penicillium</i>	70.63	94.17	94.17	117.72	376.69	211.89	729.83	141.26
<i>Phoma</i>	0	164.80	0	0	0	0	0	0
<i>Trichoderma</i>	23.54	47.09	0	0	0	0	0	0
Unknown	117.72	0	188.34	117.72	23.54	329.60	0	70.63
Yeast, miscellaneous	1,294.87	1,106.52	824.01	329.60	94.17	353.15	117.72	306.06
Total	5,932.85	4,049.39	3,084.14	1,035.90	1,600.92	2,165.98	2,825.16	2,542.66

Abbreviation: BR, bedroom.

^a Counts are expressed in colony-forming units per cubic meter except for saddle values, which are expressed in colony-forming units per gram.^b Located on the first floor.^c Located on the ground floor.

sufficient. The potential benefit of a home evaluation cannot be overemphasized. The diagnosis of HP in these siblings is supported by the typical signs and symptoms, chest CT, PFTs, BAL, serum precipitins, and recurrence of symptoms on repeated exposure. These cases represent the second report of HP resulting from nonoccupational exposure to *A pullulans* in North America and the first in children.

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