

Hypersensitivity pneumonitis due to occupational inhalation of fungi-contaminated corn dust

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Abstract: Hypersensitivity pneumonitis or extrinsic allergic alveolitis can be defined as a lung disease caused by a wide group of antigens that reach the lung by inhalation of organic and/or inorganic dust of various sources. The dust of the stored maize corn has been reported as cause of respiratory symptoms. During the storage process, maize corn dust can be contaminated by moulds and thermophilic actinomycetes, which have not been described until now as the causing antigens of these symptoms. We present a case of occupational hypersensitivity pneumonitis in an agricultural worker who cultured and stored maize corn. Clinical findings, precipitating antibodies, and evolution after having removed him from his work, confirmed the diagnosis. In our case, *Aspergillus* species contaminating the maize corn dust are probably the antigens that caused the disease.

Key words: Hypersensitivity pneumonitis, *aspergillus ssp*, maize, corn, farmer, molds, fungi

Introduction

Hypersensitivity pneumonitis (HP) or extrinsic allergic alveolitis can be defined as a lung disease caused by a wide group of antigens that reach the lung by inhalation of organic and/or inorganic dust from various sources [1, 2]. Despite extensive studies the exact immunologic mechanisms of HP are not fully known. Antigen exposure stimulates the formation of circulating IgG antibodies in exposed individuals. The clinical findings in HP with the presence of these antibodies in sera have been considered to match the concept of an immune complex-mediated reaction. HP is characterized both by proliferation of CD8+ cytotoxic lymphocytes and by an exuberant production of antibody, especially IgG, presumably from proliferation of plasma cells stimulated by CD4+ TH1 lymphocytes. Both these pathways start after inhaled antigen-carrying particles are ingested by macrophages [1, 2]. Unfortunately, many of the details of the cellular interactions that are responsible for the immunopathogenesis of HP are still obscure. The corn dust has been also involved in respiratory diseases [3, 4].

We report a case of HP due to fungi-contaminated corn dust in a farmer.

Case report

A 50-year-old non-smoking man was seen with an history of progressive dyspnoea, fatigue, unproductive cough, and chest tightness. No personal history of atopy was present. He had been working at a corn plantation for 15 years. Initially, the appearance of symptoms occurred 4 to 6 hours after occupational exposure to dust of stored corn dust, with accompanying fever, chills, and general malaise. He tolerated the green corn dust environment. On holidays these symptoms decreased but they progressively became permanent. After a weekend, the occupational exposure resulted in severe recurrence of the disease, and hospital admission was needed.

Crackles were heard on chest auscultation. Blood differential count showed 14300 leukocytes/mm³, predominantly neutrophils, without eosinophilia. Arterial blood gas determinations revealed a pH of 7.4, a PaCO₂ of 35.3 mmHg, and a PaO₂ of 60 mmHg. A chest roentgenogram showed bilateral micronodular infiltrates. Gallium-67 lung scanning showed an uptake of 67% (normal value, <60%). High-resolution computed tomography showed a diffuse "ground glass" pattern with septal thickening and small centrilobular nodules.

Pulmonary function testing showed a total lung capacity of 71% predicted, functional residual capacity of 75% predicted, forced vital capacity of 72% predicted, forced expiratory volume in 1 second of 82% predicted, and carbon monoxide diffusion in the lungs of 70% predicted. The patient exercised by Bruce's protocol, which showed arterial oxygen desaturation from 90% at baseline to 82% after 4¹/₂ minutes. Total lung capacity, as determined by plethysmography, was 71% of predicted value. Single-breath carbon monoxide diffusion test revealed a carbon monoxide transfer lung capacity of 70% of predicted value.

Bronchoscopy findings showed normal gross anatomy. Bronchoalveolar lavage (BAL) was also performed. Results of BAL fluid cultures for bacteria, fungi, and mycobacteria were negative. BAL fluid cell count showed a predominance of lymphocytes, 45%; with 40% alveolar macrophages, 10% neutrophils, and 5% eosinophils. Histological findings of a transbronchial biopsy showed mild interstitial lymphocyte infiltrate with occasional epithelioid non caseating granulomas.

Allergy study

On the basis of this information, a presumptive diagnosis of occupational HP due to corn dust was made. Skin prick tests with aeroallergens were negative, including immediate and delayed reading to the fungi skin prick tests.

As manufacturing procedures of corn storage could favour mold contamination, a fungal culture of the corn dust of our patient was performed. It showed a luxuriant growth of several species of *Aspergillus*.

A corn dust extract was made with several samples from the patient's warehouse. These samples were crushed to obtain a thin dusty material. Two grams of this dusty material were diluted in 20 ml of phosphate-buffered saline (PBS). The solution was shaken for 24 hours and then passed through a 0.22 µm Millipore filter (Millipore Corp., Bedford, Mass.). Intradermal test with this extract was positive at 6 hours. Intradermal tests with *Aspergillus fumigatus* extract was positive at 6 hours, whereas no reaction was observed to other allergens.

Total serum IgE was 50 kU/L. Specific IgE antibodies to fungi and grass pollens were assessed by CAP system (Pharmacia, Upsala, Sweden) with negative results. Precipitating antibodies IgG to fungi and grass pollens were measured by fluoride-enzyme-immuno-analysis (FEIA, CAP system, Pharmacia, Upsala, Sweden). Precipitating antibodies were detected against *Aspergillus fumigatus*, *Aspergillus clavatus* and *Aspergillus* ssp. Precipitating antibodies against the same molds were also detected in BAL fluid. Specific IgG antibodies against corn dust were not detected by the ELISA method. Precipitating antibodies against the extract of patient's corn dust were detected by the

Outcherlony method of immune-diffusion. Precipitating antibodies against corn dust were not detected. Analysis of the patient's serum did not reveal precipitins to other common antigens, including thermophilic actinomycetes. While the patient was hospitalized undergoing evaluation (with a 4-week sick leave) his symptoms decreased and his PaO₂ as determined by room air arterial blood gases increased to normal value (PO₂ 85 mmhg), with a short course of corticosteroids. Complete pulmonary function testing was normal after 6 months. He went home without any therapy. He has not resumed work, and no symptoms have been referred to date.

Discussion

HP is the result of a cell-mediated immune response of the lung to a wide variety of inhaled antigens. The mainstay of diagnosis and management is a careful exposure history and further avoidance of the causative agent if it is identified. With further clarification of the eliciting agents, molecular and immunobiologic mechanisms, and staging scheme, targeted and stage-specific therapeutic strategies might also improve clinical outcomes [2]. The most common hypersensitivity pneumonitis occurring in the farm environment is farmer's lung, which is classically caused by exposure to various thermophilic actinomycetes that grow in hay, compost, and silage [1,2]. The environmental conditions of corn dust favoured the contamination by molds. It is important to look for these agents to assess the real etiology of each case (5-9). In our patient, HP due to inhalation of fungi-contaminated corn dust was diagnosed. It illustrates the value of a site visit in the diagnosis of occupational lung disease. Clinical findings, positive precipitins, and evaluation of the patient confirmed the diagnosis without needing inhalation bronchial challenge, and ruled out the grain-dust-induced airway disease caused by endotoxin [1-4]. In our patient, the antigens of *Aspergillus* species are the etiologic agents of the HP.

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