

dently. This patient does have lymphoid tissue and normal lymphocytes and is able to respond immunologically to some types of antigens (Table II); that is, he produces IgG antibody to protein and IgE to pollens, dust mites, and *A. fumigatus*. Therefore it appears that his antibody deficiency is likely to be due to immune dysregulation, a phenomenon that presumably could be involved in ABPA. Alternative to this idea would be the concept that just as autoimmunity may accompany common variable immune deficiency, this case illustrates that hypersensitivity can accompany it as well.

The prevalence of ABPA in the United States has been a source of contention.<sup>4-6</sup> Typically, many more cases are reported from the United Kingdom than from the United States, but there appear to be regional areas of the United States, such as the Great Lakes, where more cases are reported than elsewhere in the United States. One may question the role of prolonged intermittent steroid therapy, which this patient had throughout his adult life, in the development of immune deficiency syndrome, but the possible causal relationship of steroids in the development of immune hyporesponsiveness has been argued and is an issue that has not been settled. We cannot determine whether the steroid therapy for his asthma and ABPA played a role in

the development of his immune deficiency syndrome. Recognition of these two clinical entities in a single patient clearly requires a combination of careful clinical follow-up and detailed use of the clinical immunology laboratory to prove the existence of any such syndromes. Once recognized, treatment is usually straightforward, and as seen in our patient, will lead to a marked improvement in the clinical course.

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## Hypersensitivity pneumonitis in a patient with hypogammaglobulinemia

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Hypersensitivity pneumonitis (HP) is an inflammatory disease of the lung parenchyma, which occurs in a susceptible host after repeated inhala-

#### Abbreviation used

HP: Hypersensitivity pneumonitis

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tion of a multitude of antigens.<sup>1</sup> Although immunologically mediated, the relative contributions of cellular versus humoral immunity in the pathogenesis of HP remain undefined. We report here an "experiment of nature," a patient with simultaneous agammaglobulinemia and HP. This case report illustrates that specific antibody is not required for clinical HP and supports the central role of cellular immunity in mediating HP.

TABLE I. Pulmonary functions

|                    | Admission |        |       | One Year Later |       |
|--------------------|-----------|--------|-------|----------------|-------|
|                    | Pred      | Actual | %Pred | Actual         | %Pred |
| TLC                | 5.08      | 3.99   | 79%   | 4.48           | 88    |
| TGV                | 2.85      | 2.54   | 89%   | 2.89           | 101   |
| RV                 | 1.23      | 1.23   | 100%  | 1.29           | 105   |
| FVC                | 3.85      | 2.67   | 69%   | 2.69           | 70    |
| FEV <sub>1</sub>   | 3.11      | 2.45   | 79%   | 2.33           | 75    |
| FEV <sub>1</sub> % | 81        | 92     | 114%  | 87             | 109   |
| DLCO               | 27.0      | 16.78  | 62%   | 27.1           | 97    |
| DLCO/VA            | 5.4       | 4.4    | 81%   | 6.2            | 110   |

Abbreviations: TLC, Total lung capacity; TGV, thoracic gas volume; RV, residual volume; FVC, forced vital capacity; FEV<sub>1</sub> %, FEV<sub>1</sub>/FVC × 100, DLCO, single-breath diffusing capacity of the lung for carbon monoxide; DLCO/VA, (corrected for hemoglobin), DLCO corrected for lung volume.

## CASE REPORT

A 44-year-old female homemaker with a history of mild asthma and chronic sinusitis was first seen for evaluation of low-grade fevers, dyspnea, and nonproductive cough of several weeks' duration. The patient had no history of cigarette use or unusual hobbies. Physical evaluation was remarkable for bi-basilar rales without wheezing.

Results of laboratory evaluation were as follows: room air arterial blood gas, pH 7.44; PO<sub>2</sub>, 51; PCO<sub>2</sub>, 34; and A-a gradient, 31. The chest radiograph showed fine, reticulonodular, lower-lobe interstitial infiltrates. Pulmonary function tests showed a mild restrictive defect with a reduced single-breath diffusing capacity of the lung for carbon monoxide (Table I). Bronchoalveolar lavage demonstrated 50% lymphocytes (CD4, 50%; CD8, 42%), 30% macrophages, 18% neutrophils, and 2% eosinophils. Results of chest computed tomographic scan (Fig. 1) and thoracoscopic lung biopsy examination (Fig. 2) were consistent with HP. Serum precipitins measured by immunodiffusion with threefold concentrated serum for the following antigens were negative: *Taenia vulgaris*, *Micropolyspora feani*, *Candida* spp., pigeon serum, *Aureobasidium pullulans*, *Aspergillus* mix, *Stemphylium* spp., *Streptomyces* spp., *Trichoderma* spp., *Verticillium* spp., *Alternaria* spp., *Cladosporium* spp., *Epicoccum* spp., *Fusarium* spp., *Geotrichum* spp., *Helminthosporium* spp., *Curvularia* spp., *Mucor* spp., *Penicillium* spp., *Rhizopus* spp., and *Scopulariopsis* spp. Cultures for bacteria and fungal and viral pathogens were negative.

Humoral immunity was evaluated because of the presence of severe, chronic sinusitis and revealed an IgG of 184 mg/dl (normal value, 706 to 1451 mg/dl), an IgA of 22 mg/dl (normal value, 78 to 340 mg/dl), and an IgM of 123 mg/dl (normal value, 52 to 280 mg/dl). The patient made no specific antibody in response to vaccination with diphtheria and tetanus toxoids, pneumococcal polyvalent vaccine, and *Haemophilus influenza* type b diphtheria-conju-



FIG. 1. Thoracic computed tomographic scan of the chest. Lung parenchyma is diffusely abnormal with patchy, hazy increase in lung density with fine nodularity. Although not shown, mediastinal windows were normal without lymphadenopathy.

gate vaccine. The number of B cells was low (12 cells/mm<sup>3</sup>), and the number of T cells was normal.

The patient's clinical picture was believed to be most consistent with a diagnosis of HP with co-existent common variable immunodeficiency (acquired hypogammaglobulinemia). She was initially treated with 60 mg of prednisone per day and experienced dramatic relief of symptoms within a few days with concomitant reduction of her A-a gradient, which decreased from 31 to 19. The patient was discharged with a prescription for prednisone, 40 mg, but returned 4 days later with low-grade fevers, increasing dyspnea, and nonproductive cough. She was re-admitted, and her condition improved without any change in therapy within a few days. She was discharged but again experienced symptoms within 3 days. The patient had moved into a new home 4 weeks before the onset of her illness. An environmental assessment of her home failed to reveal the sensitizing antigen. The patient has not returned to this home since her last admission. Without steroid therapy for over 3 years, she has had complete resolution of her respiratory symptoms. Results of pulmonary function tests 1 year after her hospital admission had returned to baseline values (Table I). Her hypogammaglobulinemia persists, and she requires maintenance therapy with intravenous gamma globulin.

## DISCUSSION

Most patients with HP exhibit serum precipitating antibodies directed against the offending antigen, and many investigators believe that HP is an immune complex-mediated disease. However, bronchoalveo-

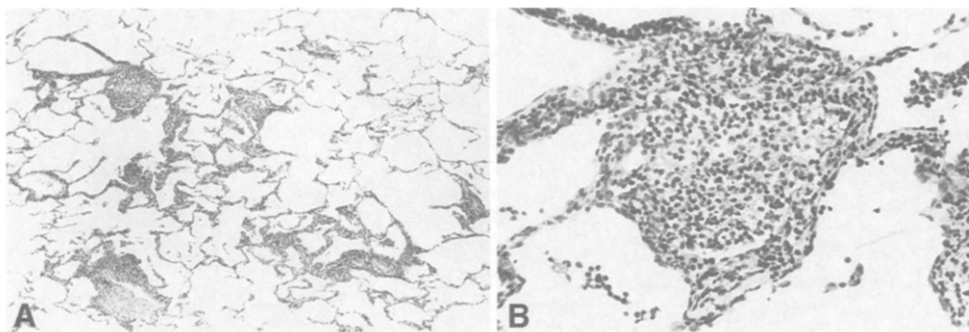


**FIG. 2.** Lung biopsy specimen shows patchy interstitial and bronchiolar lymphocytic infiltrate with granulomatous infiltration. (Original magnifications,  $\times 22$  and  $\times 220$ .)

lar lavage of patients with HP shows T-cell lymphocytosis,<sup>2</sup> a striking increase in the number of mononuclear cells in the lung parenchyma, and the formation of pulmonary granulomata<sup>3</sup>; the latter feature is characteristic of T-cell-mediated, delayed-type hypersensitivity reactions. Murine models further dispute the etiologic role of precipitating antibodies in mediating HP.<sup>4,5</sup> These studies demonstrate that experimental HP can be transferred by CD4<sup>+</sup> T cells but not by either B cells or antibodies directed against the sensitizing antigen, *M. feani*.

We believe that this case report of HP with coexistent hypogammaglobulinemia illustrates the essential role of cellular and not humoral mechanisms in the pathogenesis of this disorder. Patients with common variable immunodeficiency have markedly depressed serum immunoglobulin levels and are unable to produce specific antibody in response to immunization. The latter feature helps distinguish common variable immunodeficiency from a variety of disorders in which immunoglobulin levels are moderately depressed but humoral immunity is otherwise intact. The absence of serum precipitins in this patient with HP reflects the general inability of patients with common variable immunodeficiency to

produce specific antibodies in response to challenge by exogenous antigens.

The patient presented here is, to our knowledge, the first reported case of HP co-existent with common variable immunodeficiency. This case supports the hypothesis that HP results from aberrant T-cell-mediated immunity, independent of precipitating antibody.

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