

Case report

Eosinophilic pneumonia caused by *Alternaria alternata*

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We describe a patient who presented with hypoxemia and diffuse bilateral pulmonary infiltrates. The diagnosis of eosinophilic pneumonia was confirmed by bronchoalveolar lavage and transbronchial lung biopsy. The remarkable characteristic was reappearance of the symptoms on the patient's return home, suggesting the existence of etiologic agents in his house. An environmental survey of the patient's house yielded *Alternaria alternata*. A high titer of anti-*A. alternata* antibody (IgG) was detected in his serum, and the inhalation bronchoprovocation test with *A. alternata* antigen was positive. This case indicates that *A. alternata* is a probable cause of eosinophilic pneumonia.

Key words: *Alternaria alternata*; bronchoprovocation test; environmental survey; eosinophilic pneumonia.

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Eosinophilic pneumonia is defined as pulmonary infiltration of the lung by eosinophils that may or may not be accompanied by an excess of these cells in the peripheral blood. When the causative substances cannot be detected, i.e., the disorder is idiopathic, the diagnosis would be acute or chronic eosinophilic pneumonia according to the clinical course. In some patients with eosinophilic pneumonia, the causative substrates can be detected: drugs (1), parasitic and fungal infection (2–4), bronchopulmonary aspergillosis (5), and so on.

Although it is well known that *Alternaria alternata* spore antigen is one of the aeroantigens causing allergic rhinitis and bronchial asthma (6), there have been no reports that the antigen causes eosinophilic pneumonia. We present here the first case of subacute onset eosinophilic pneumonia induced by the *A. alternata* antigen.

Case report

A 65-year-old man was admitted to our hospital on 31 March 1994 because of dry cough, dyspnea

on exertion, and high-grade fever. Twelve days before admission, he had consulted a physician, was diagnosed as having "acute bronchitis", and treated with antibiotics. Further questioning revealed that the patient had been healthy without history of atopic diseases until the onset of the present illness. He was a fisherman and lived with his family in a 40-year-old wooden house with little direct sunlight. He was a smoker (25 cigarettes/day for 45 years) and did not drink alcoholic beverages.

Physical examination revealed the following: temperature 38.2°C; blood pressure 130/80 mmHg; heart rate 90 beats/min. Cardiac examination was entirely within normal limits. Auscultation of the lungs revealed late inspiratory fine crackles bilaterally without wheezes or rhonchi.

Abnormal laboratory studies included arterial blood gas levels while breathing room air: P_{aO_2} 66.1 mmHg; P_{aCO_2} 31.0 mmHg. The white blood cell count (WBC) was 12 800/ μ l with a differential of 69.4% neutrophils, 20.2% lymphocytes, 4.8% monocytes, and 5.4% eosinophils. The erythrocyte sedimentation rate was 103 mm/h. The C-reactive

protein (CRP) was 13.8 mg/dl, and the IgE level was 1067 U/ml. Skin tests or specific IgE antibodies to 10 common aeroallergens, including *Aspergillus fumigatus*, were negative. The following laboratory findings were normal or negative: urinalysis; stools for ova and parasites; serum electrolytes; total protein albumin; and bacterial, mycobacterial, and fungal cultures of the sputum.

Chest radiographs on admission (Fig. 1) showed diffuse reticulonodular shadows on the bilateral lung fields. The computed tomographic (CT) chest scan on admission (Fig. 2) showed diffuse, ground glass-like opacities with fine reticulonodular shadows in both lung fields.

The pulmonary function test performed by the Collins DS system, according to the standards of the American Thoracic Society (7), revealed FVC 2.37 l (75.2% of predicted value), FEV₁ 1.91 l (87.2% of predicted value), FEV₁/FVC ratio 80.6%, TLC 3.13 l (62.5% of predicted value), RV 0.91 l (62.8% of predicted value), DLco 6.47 ml/min/mmHg (49.5% of predicted value), and DLco/VA 2.49 ml/min/mmHg/l (54.1% of predicted value).

Differential cell analysis of bronchoalveolar lavage fluid (BALF) revealed 58.0% alveolar macrophages, 3.0% lymphocytes, 0.0% neutrophils, 39.0% eosinophils, and an increased total cell count of 5.0×10^6 cells/ml. Histologic examination of trans-bronchial lung biopsy (TBLB) specimens obtained from the right S⁸a (Fig. 3) showed alveolar septal thickening with eosinophil infiltration and intraluminal organization.

Two days after admission, the patient promptly improved with 20 mg/day prednisolone, and the steroid therapy was tapered and discontinued on 15 April. For investigation of environmental causes, he returned home on 16 April, and a recrudescence occurred on the next day: recurrence of dry cough, increases in CRP (from 1.07 to 2.83 mg/dl) and WBC (from 12 100 to 13 900/ μ l), and decreases in PaO₂ (from 86.4 to 80.1 mmHg) and DLco (from 8.25 to 7.00 ml/min/mmHg), indicating that the environmental provocation test was positive. We advised him to clean his entire house. As his symptoms promptly disappeared spontaneously, he was discharged on 26 April.

From the sterile Petri dishes containing Sabouraud's agar medium supplemented with antibiotics, exposed for 10 min on the floor of every room in the patient's house with closed windows, *A. alternata* was isolated in the living room, and *Phoma hibernica* in the Buddha room.

The specific IgE antibody against *A. alternata* (RAST) was negative in his serum. For the preparation of fungal antigenic solutions, each fungus antigen (polysaccharide) was cultured on the medium (1% peptone, 2% glucose) with 0.5% yeast extract

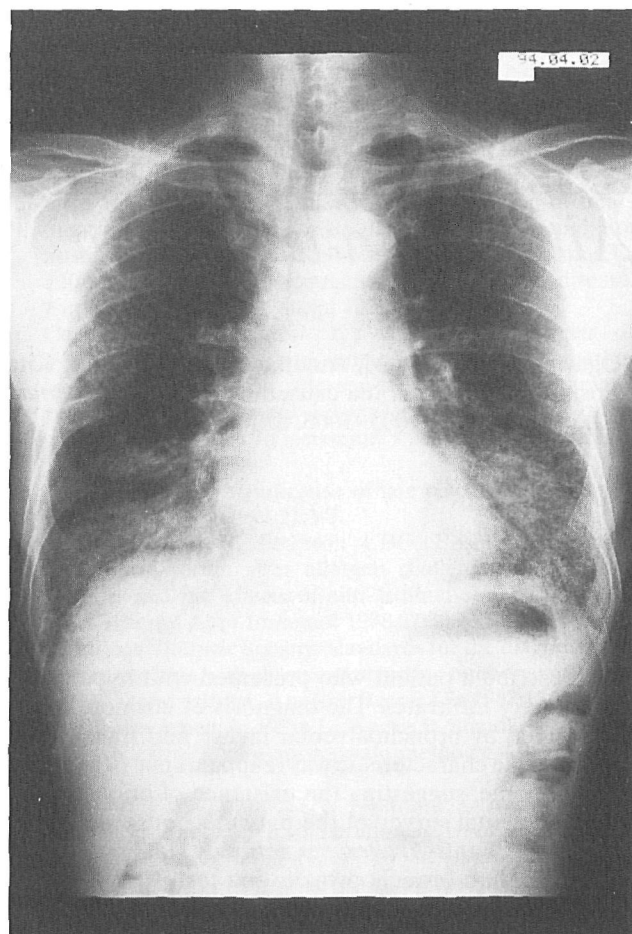


Fig. 1. Chest radiograph on admission showing diffuse reticulonodular shadows on bilateral lung fields.

for 20 days and dried by acetone. Skin tests with the fungal antigens were done by intradermal injection of 0.02 ml of the antigen solution (1 mg/ml). Both the immediate (15 min)- and delayed (48 h)-type skin reactions were weakly positive for *A. alternata*, but negative for *P. hibernica*. The serum antifungus antibody titers referred to IgG measured by the Ouchterlony method were $\times 16$ for *A. alternata* and $\times 4$ for *P. hibernica*.

On 14 November 1994, the patient was admitted for the bronchoprovocation test with *A. alternata* antigen, having given his informed consent. The provocation test was approved by the ethics committee of our hospital, to whom we explained that the test was necessary for definite diagnosis and to plan the appropriate therapy. The culture-filtrate antigen (1 mg/ml) in a dose of 2 ml was inhaled by tidal mouth breathing from a Devilbiss 646 nebulizer (Devilbiss Co, Somerset, PA, USA), operated by compressed air at 5 l/min. The result was considered positive; a development of dry cough within 6 h, significant decreases in PaO₂ (from 95.5 to 85.3 mmHg) and DLco (from

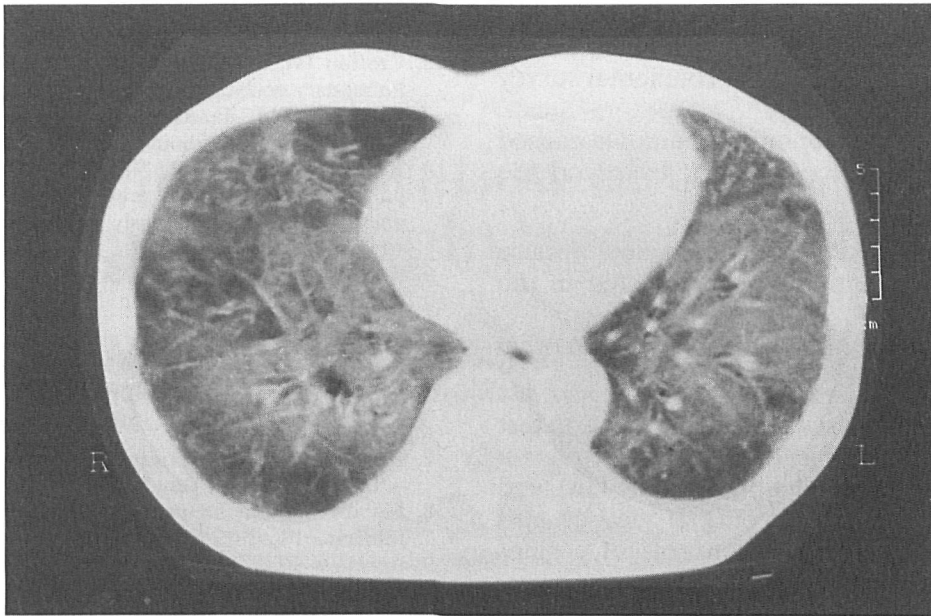


Fig. 2. Chest CT scan on admission showing diffuse ground glass opacities with small granular shadows in both lung fields.

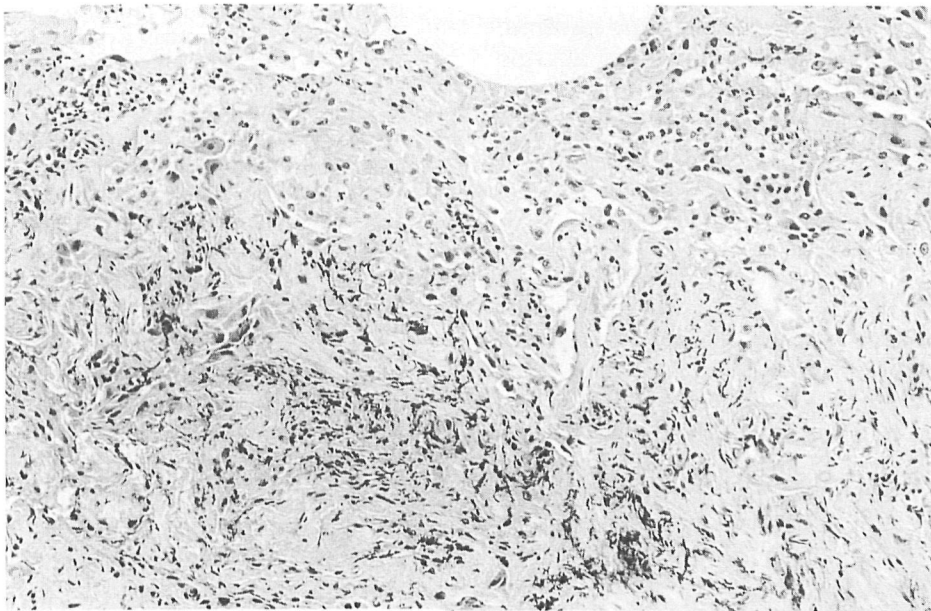


Fig. 3. Histology of transbronchial lung biopsy specimens obtained from right S⁸a, showing alveolar septal thickening with eosinophil infiltration and intraluminal organization.

8.25 to 7.00 ml/min/mmHg), and an increase in CRP in the serum (from 0.15 to 1.33 mg/dl) on the day after the test. The FEV₁ value decreased from 2.10 to 2.02 l, suggesting no significant bronchoconstrictor response to the antigen. These symptoms and signs disappeared within 5 days after the challenge.

On the basis of these results, we once more advised the patient to clean his house, especially the room contaminated with *A. alternata*. We have followed up this case carefully, and the patient has been healthy without any recurrence for the last 3 years.

Discussion

Eosinophilic pneumonia has been defined by Liebow & Carrington (8) as pulmonary infiltration of the lung by eosinophils that may or may not be accompanied by an excess of eosinophils in the peripheral blood. Although a number of etiologic agents (9–11) have been described, the cause is unknown in most cases. As well-known causes of eosinophilic lung diseases (12) were easily eliminated and the symptoms reappeared when our

patient returned home, the existence of some etiologic agents in the patient's house was suggested. Therefore, we carried out an environmental survey of the house.

The diagnosis of eosinophilic pneumonia caused by *A. alternata* in our patient was based on the following facts:

- 1) *A. alternata* was isolated from the patient's house
- 2) anti-*A. alternata* antibody was detected in the serum
- 3) the bronchoprovocation test (13) to *A. alternata* antigen was positive.

It is recognized that the bronchoprovocation test is useful in diagnosing farmer's lung (14), pigeon breeder's disease (15), malt worker's lung (16), and hypersensitivity pneumonitis (17). It may be also useful in determining etiologic agents of eosinophilic pneumonia.

A. alternata grows principally on leaf surfaces and organic debris. The dry spores float in the air and are inhaled. Although the spores are prominent throughout the growing season, the peak levels are said to occur in late summer and autumn. It is well known that the spores can cause allergic rhinitis and bronchial asthma (6), but, to our knowledge, there has been no report of eosinophilic pneumonia caused by *A. alternata*. Our case indicates that *A. alternata* should be considered an etiologic agent of eosinophilic pneumonia.

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