Invasive pulmonary aspergillosis complicating allergic bronchopulmonary aspergillosis

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Invasive pulmonary aspergillosis is a frequent complication in immunocompromised patients. The role of the prolonged use of steroids in predisposing to invasive aspergillosis has been recognized, but exceptionally described in asthmatic patients. We report the case of a 59-year-old woman with bronchial asthma treated with steroid therapy for a long time, who developed an invasive pulmonary aspergillosis with an unusual combination of invasive and allergic disease. It seems reasonable to think that allergic disease due to allergic bronchopulmonary aspergillosis (ABPA) preceded the terminal invasive process. Adjunctive therapy with antifungal agents in patients with ABPA is considered, since there is the risk of an invasive pulmonary aspergillosis.

Introduction

Aspergillus species are among the most common fungi encountered by humans, and the ability of these moulds to evoke disease depends on the local or general physiologic and immunologic state of the host (1). Aspergillus lung disease takes several forms: allergic reactions, saprophitic and invasive infections. Invasive pulmonary aspergillosis normally occur in abnormal lungs or in association with leukaemia, lymphoma or in immunocompromised patients after cytotoxic treatment or high-dose corticosteroid therapy. Recently many cases of invasive pulmonary aspergillosis are reported in non-immunocompromised patients (2-4). We describe a case of fatal invasive pulmonary aspergillosis complicating steroid-dependent asthma in a patient with clinical findings highly suggesting invasive and allergic disease due to Aspergillus species.

Case Report

A 59-year-old woman was admitted to the hospital with a 1-week history of breathlessness and fever. Her medical history was unremarkable except for bronchial asthma most of the time treated with oral steroids (average dose was prednisone 10 mg day−1 for 2 yr) and inhaled β2-agonists. The chest X-ray showed diffuse bilateral alveolar shadowing (Plate 1) and the physical examination revealed fine inspiratory crackles. Her blood pressure was 150/90; pulse rate 95 beats min−1; respiratory rate 30 breaths min−1; temperature 37.5°C. Laboratory findings showed an arterial pH of 7.48, PCO2 of 32 mmHg, PO2 of 58 mmHg on room air; white blood cell count of 14,000 with 75% neutrophils and 8% eosinophils, erythrocyte sedimentation rate 55 mm hr−1. Cultures of sputum, urine, blood and stool were taken and all remained negative. Antibody titres of Mycoplasma pneumoniae, Legionella pneumophila, Clamydia psittaci and influenza viruses A and B were low; the remainder of laboratory findings were normal and HIV seroconversion was absent. She was empirically treated with broad-spectrum antibacterial therapy (ceftazidime and erythromycin) and received oxygen by face mask. On the second day a bronchoalveolar lavage (100 ml total) and a transbronchial biopsy were performed. The bronchoalveolar lavage cell differential count revealed 10% eosinophils, 10% lymphocytes and 80% macrophages. The main histologic features observed in the biopsy were pulmonary granulomas containing fungal organisms with septae hyphae. Special stains of bronchoalveolar lavage revealed large numbers of fungal colonies morphologically characteristic of Aspergillus species (Plate 2). These were confirmed by post mortem culture to be Aspergillus fumigatus. Precipitating antibodies to Aspergillus fumigatus were positive (+++) in peripheral blood and total serum IgE were more than 2000 UI L−1, with specific IgE antibodies to antigens of Aspergillus species. The day after the bronchoscopy, therapy with amphotericin B was

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begun but, because of acute respiratory failure, the patient was admitted to the intensive care unit, intubated and mechanically ventilated; nevertheless she died 2 days later.

**Discussion**

Although serious infectious complications, especially fungal infections, are often associated with long-term high-dose steroid therapy for exacerbations of chronic obstructive pulmonary disease (4,5) invasive pulmonary or disseminated aspergillosis is a rare complication in asthmatic patients (6,7) and exceptionally described in patients with allergic broncopulmonary aspergillosis (ABPA) (8–11). Our patient had a history of steroid-dependent asthma with peripheral eosinophilia, eosinophilic alveolitis (as assessed by bronchoalveolar lavage) and serum precipitating anti-*Aspergillus* antibodies together with high titres of total and specific antibodies of IgE class. Unexpectedly these findings were observed while the patient also had evidence of invasive pulmonary aspergillosis, although they are not usually associated to such a condition. Pulmonary and
Peripheral eosinophilia with high serum levels of total and specific IgE antibodies in a chronic asthma sufferer who developed invasive aspergillosis suggest the hypothesis that the latter overlapped with ABPA. In this view it seems reasonable to think that ABPA preceded the terminal invasive process caused by the fungus. Corticosteroids are the therapy of choice of ABPA, but steroid treatment is an important risk factor for invasive pulmonary aspergillosis (12). Limited tissue invasion with granuloma has been described as a possible complication of steroid therapy in ABPA (8,13). Such semi-invasive aspergillosis in patients with ABPA during steroid therapy is probably due to the low dose of steroids needed to control their symptoms but also the capability of the hypersensitivity host response to limit the fungal invasion. Our patient developed a fatal invasive pulmonary aspergillosis during steroid treatment (prednisone 10 mg day⁻¹). This dose is frequently used in patients with asthma and, despite the adverse effects of these drugs on host defences against invasion by Aspergillus sp., the risk of an invasive fungal infection in such a setting is probably quite low (11). It is not clear whether an adjunctive therapy with antifungal agents can give benefit to reduce clinical symptoms in ABPA (14). It has been suggested that an antifungal therapy should be considered in patients treated with steroids when progressive pulmonary infiltrates do not respond to conventional antimicrobial therapy (2). In our opinion at that time, it is too late to prevent a possible fatal course of an invasive aspergillosis.

References