Nosocomial outbreak of *Aspergillus fumigatus* infection among patients in a renal unit?

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**Abstract** *Aspergillus fumigatus* is present in the environment worldwide and it is only able to infect debilitated or immunodepressed subjects. Nosocomial outbreaks of *A. fumigatus* infection have been associated with hospital reconstruction. Spores are released into the environment and are inhaled by immunodepressed patients housed in nearby Medical Units. Specific clinical syndromes are allergic bronchopulmonary aspergillosis and invasive pulmonary aspergillosis with characteristic radiological features. Invasive *A. fumigatus* infection is commonly fatal, even if promptly diagnosed and treated. Three consecutive cases of *A. fumigatus* infection occurred in debilitated patients housed in our Renal Unit while building renovation near the Unit was being performed. Two of these patients died and pulmonary and diffuse aspergillosis was found on postmortem examination. The third patient, highly suspected to be infected with Aspergillus, was aggressively and successfully treated with liposomal amphotericin B. Our experience suggests that fungal infections have gained increasing prominence in clinical medicine and they must be considered in chronic debilitated patients including dialysis patients, and that liposomal amphotericin B represents an important advance in the treatment of aspergillosis.

**Key words:** *Aspergillus fumigatus* infection; immunodepression; liposomal amphotericin B

**Introduction**

*Aspergillus fumigatus* infections are often life-threatening and unresponsive to antifungal treatment. Infection follows the inhalation of spores released into the environment and many cases of nosocomial outbreaks of aspergillosis have been associated with hospital reconstruction near Medical Units in which immunodepressed patients are housed [1,2].

Although hundreds of *Aspergillus* species are known, only a few are pathogenic to humans. *Aspergillus fumigatus* is the most common [3,4] and infections occur worldwide without regard to race, sex, age, and are increasing in prevalence among immunodepressed subjects. *Aspergillus* is not transmitted from human to human. Conidia are present in the air and are constantly being inhaled.

The effectiveness of normal host defences explains the rarity of the disease: macrophages are responsible for the killing of conidia, whereas neutrophils fight mycelia. However, even isolated neutrophil defects such as those associated with granulomatous disease, intense immunosuppression, the use of various antibacterial drugs for septic episodes, or every chronic pathological condition that compromises the host defences, are characterized by an increased incidence of pulmonary infection by *Aspergillus* species.

Amphotericin B is the treatment of choice for invasive pulmonary aspergillosis [5], despite several side-effects associated with this drug. Encapsulation of amphotericin B into liposomes appears to improve the clinical efficacy and to reduce the toxic side-effects [6–8]: liposomal amphotericin B represents an important advance in the treatment of invasive pulmonary aspergillosis and it might be proposed as prophylaxis [9].

We report herein three cases of invasive opportunistic pulmonary infections, two of which were certainly, and another presumably, due to *A. fumigatus* which recently occurred in debilitated patients housed in our Department of Nephrology and Dialysis, while building renovation work near the Unit was in progress.

**Case reports**

**Case 1**

A 85-year-old female, treated with CAPD for 31 months because of chronic renal failure due to nephrosclerosis, was admitted to the hospital in January 1995 for acute pneumonia with remittent hyperpyrexia. She had been recently treated with co-trimoxazole for peritonitis due to *Enterobacter clo-
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Case 1

*acae*, after a course of gentamicin failed to resolve the infection. A radiograph of the chest showed a pulmonary infiltrate in the left retrocardiac region. The subsequent clinical course was characterized by respiratory failure in the absence of fever, leukocytosis, cough and expectoration; the radiological picture evolved into the formation of multiple small pulmonary bilateral infiltrates. In spite of the antibiotic treatment, she died on the 10th hospital day. Histological examination revealed aspergillus hyphae in the multiple pulmonary nodules (Figure 1).

Case 2

A 49-year-old female with Wegener granulomatosis, who had been previously treated with methylprednisolone pulses and currently with oral prednisone plus azathioprine, was admitted in February 1995 because of cough and fever (38.5–39.5°C). A radiograph of the chest showed a cavitary pulmonary lesion in the left axillary region. The radiological picture rapidly evolved into the formation of multiple bilateral infiltrates. Bronchoscopic examination with biopsy revealed ulcerative lesions of the bronchial tree. A CT scan of the chest confirmed the presence of multiple pulmonary bilateral infiltrates. The patient was not febrile, coughing, or producing sputum; the WBC count was normal. Repeated cultures of sputum and blood yielded negative results, and serological examinations were also negative. He was initially treated with broad-spectrum antibacterial therapy with no improvement; a CT-guided lung biopsy was ineffective. A presumptive diagnosis of aspergillosis was made and liposomal amphotericin B was initiated with no radiological improvement for at least 20 days. The dose was increased to 3 mg/kg and on the 36th day of hospitalization the patient was discharged with amphotericin B pulse therapy (6 mg/kg per day every 72 h) and rifampicin (18 mg/kg per day). The radiographic picture was improved on the 26th day of antifungal treatment and a CT scan performed 10 weeks after the onset demonstrated amelioration and almost complete regression of the pulmonary infiltrates (Figures 3, 4).

Case 3

A 65-year-old male, treated with CAPD for chronic renal failure due to renal vascular disease, developed severe malnutrition and was admitted in February 1995. Physical findings indicated pneumonia, which was confirmed by thoracic radiographs that showed multiple pulmonary bilateral infiltrates. The patient was not febrile, coughing, or producing sputum; the WBC count was normal. Repeated cultures of sputum and blood yielded negative results, and serological examinations were also negative. He was initially treated with broad-spectrum antibacterial therapy with no improvement; a CT-guided lung biopsy was ineffective. A presumptive diagnosis of aspergillosis was made and liposomal amphotericin B was initiated with no radiological improvement for at least 20 days. The dose was increased to 3 mg/kg and on the 36th day of hospitalization the patient was discharged with amphotericin B pulse therapy (6 mg/kg per day every 72 h) and rifampicin (18 mg/kg per day). The radiographic picture was improved on the 26th day of antifungal treatment and a CT scan performed 10 weeks after the onset demonstrated amelioration and almost complete regression of the pulmonary infiltrates (Figures 3, 4).

Fig. 1. Pulmonary nodule with aspergillus hyphae from patient 1.

Fig. 2. Multiple cerebral foci of aspergillosis in patient 2.

Fig. 3. CT scan obtained on admission in patient 3, demonstrating multiple pulmonary parenchymal nodules.
Fig. 4. CT scan obtained 10 weeks after the onset and after 4 weeks of treatment with liposomal amphotericin B in patient 3, demonstrating almost complete regression of the pulmonary infiltrates.

Discussion

Our report constitutes suggestive but not definitive evidence of nosocomial transmission of *A. fumigatus* infection, because we cannot definitely exclude a coincidental cumulation of cases. However, this clustering of cases is remarkable, given the very low incidence and prevalence of invasive fungal infection in our hospital. The exact data are not available because these infections are often misdiagnosed and no environmental control by air sampling of Aspergillus spores was performed, since this is not believed to be a sensitive approach.

Our experience, even if unfortunate, has been important for a number of reasons.

First, hospital construction or renovation work, in or near Units where immunodepressed or debilitated patients are housed should alert physicians to the possibility of an outbreak of aspergillosis, usually due to *A. fumigatus*.

Secondly, fungal infections should be considered in Wegener granulomatosis patients receiving immunosuppressive therapy and who present with pulmonary symptoms. Moreover, elderly or debilitated patients undergoing chronic dialysis treatment are also susceptible to invasive *A. fumigatus* pulmonary infection when favourable conditions arise.

Thirdly, the cause of radiologically apparent, multiple nodules should be promptly diagnosed and if fungal infection is suspected, treatment with amphotericin B should be initiated. The unilamellar liposomal amphotericin B is safe to administer, and results regarding its efficacy in eradicating invasive *A. fumigatus* infection are encouraging [8].

Finally, hospital Units in which immunodepressed patients are housed should have an efficient ventilation system with filtered air.

References


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