

Locally invasive pulmonary aspergillosis occurring in a gardener: an occupational hazard?

J A ZUK, D KING, H D ZAKHOUR, J C DELANEY

From the Departments of Histopathology and Medicine, Arrowe Park Hospital, Upton, Merseyside

ABSTRACT Fatal locally invasive pulmonary aspergillosis occurred in a previously fit young patient who had no predisposing factors other than exposure to fungal spores in his occupation as a gardener.

Invasive pulmonary aspergillosis is uncommon, usually occurring in immunocompromised patients or in those with abnormal lungs. We describe a fatal case occurring in a previously fit young man.

Case report

A 34 year old man was admitted as an emergency with a five day history of dyspnoea, unproductive cough, fever, and anorexia. He had worked as a gardener for 14 years and had never left Britain. He was heterosexual and denied intravenous drug abuse. Five months previously he had had an episode of salmonella gastroenteritis, when a routine chest radiograph was normal. On examination he had central cyanosis and pyrexia (38°C). His respiratory rate was 40/min and heart rate 120/min. Chest auscultation indicated fine inspiratory crackles and bronchial breath sounds at both bases. A chest radiograph showed bilateral basal alveolar shadowing. Initial blood gas measurements when he was breathing air were: arterial oxygen tension (Pao₂) 8.4 kPa, arterial carbon dioxide tension (Paco₂) 4.9 kPa, pH 7.43. There was a neutrophil leucocytosis (16 × 10⁹/l). He was treated with intravenous fluids, erythromycin 1 g four times daily, physiotherapy, and continuous 75% inspired oxygen. After 48 hours he remained febrile and gentamicin 80 mg thrice daily and co-trimoxazole 960 mg twice daily were added.

After seven days the basal shadowing on his chest radiograph had become more extensive and fiberoptic bronchoscopy and bronchial biopsy were carried out. Histological examination showed extensive replacement of the bronchial wall by epithelioid granulomas showing small central foci of necrosis and surrounded by neutrophils, plasma cells, and lymphocytes. Neither fungi nor acid fast bacilli were seen. Prednisolone 40 mg/day and antituberculous treatment (rifampicin, isoniazid, ethambutol, and pyrazinamide) were started. The Mantoux test and blood and sputum cultures gave negative results. Paired titres of antibodies to *Mycoplasma pneumoniae*, *Legionella pneumophila*, and a range of pulmonary viral pathogens showed no appreciable rise, and screening for human immunodeficiency virus gave a negative result. On the 19th day his condition deteriorated; radiogra-

Address for reprint requests: Dr A J Zuk, Department of Histopathology, Arrowe Park Hospital, Upton, Merseyside L49 5PE.

Accepted 13 May 1989

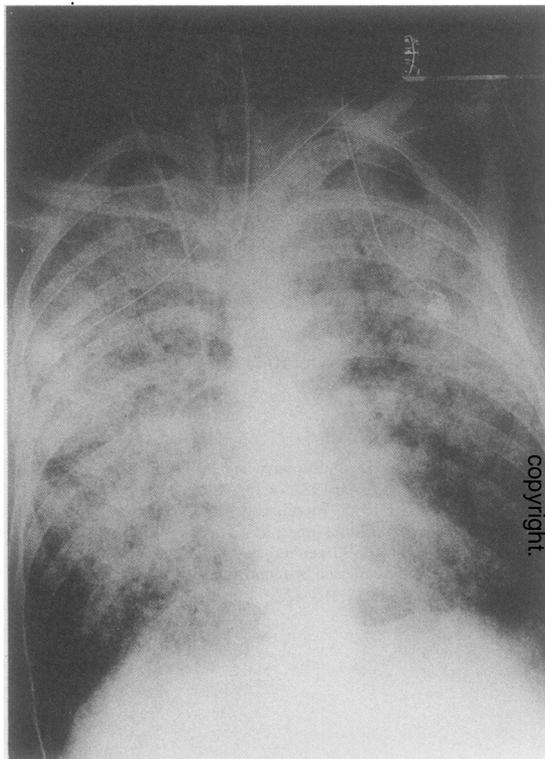


Fig 1 Chest radiograph 48 hours before death.

phy showed extensive bilateral shadowing (fig 1) and with 100% oxygen Pao₂ was 6.3 kPa, Paco₂ 4.7 kPa, and pH 7.49. Assisted ventilation was instituted but he remained severely hypoxaemic and died 48 hours later (21 days after admission). *Aspergillus fumigatus* was isolated from sputum 24 hours before death. *Aspergillus precipitans* were absent.

At necropsy substantial changes were present in the respiratory system only. There were bilateral fibrinous pleural adhesions and serous effusions (each 300 ml). Both lungs were extremely heavy, with blood stained mucus in the bronchi. All lobes were diffusely consolidated by innumerable miliary yellow and grey necrotic and suppurative foci which were individually 0.5-1.0 cm in diameter but were becoming confluent in places. Hilar and lower paratracheal lymph nodes were enlarged. Histologically all lobes showed extensive parenchymal destruction as a result of a mixed acute and chronic inflammatory cell infiltrate that included epithelioid cells with granulomas and giant cells (fig 2). Large

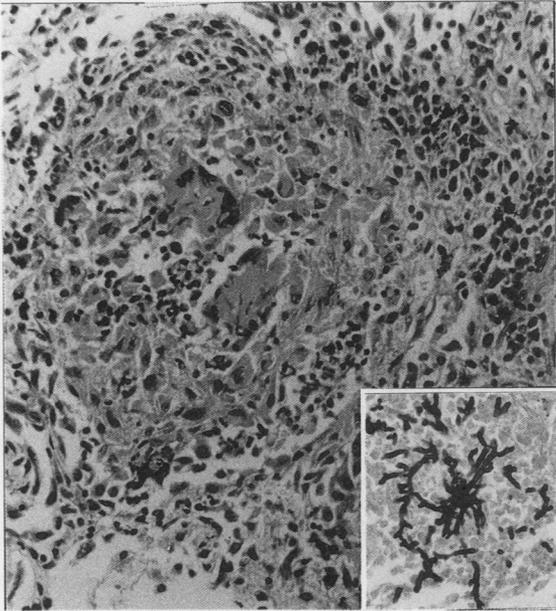


Fig 2 Destructive granulomatous pulmonary inflammation; the fungal hyphae are morphologically *Aspergillus* sp. (Inset: Grocott stain.)

numbers of fungal colonies morphologically characteristic of *Aspergillus* sp were found throughout (fig 2, inset). These were confirmed by postmortem culture to be *A fumigatus*. Fungal hyphae were also present within giant cells. Neither vascular invasion by fungi nor vasculitis was present. Lymph nodes showed reactive changes only and fungi were not found outside the lungs. No acid fast bacilli were seen.

Discussion

Aspergillus lung disease takes several forms, these being allergic reactions or saprophytic and invasive infections.¹ Of all these forms, invasive pulmonary aspergillosis is least common, normally occurring in abnormal lungs (for example, cysts, old tuberculous cavities) or in association with leukaemia, lymphoma, and carcinoma and in patients having high dose corticosteroid or cytotoxic treatment—that is, in the immunocompromised host.^{2,3} Our patient had none of these predisposing factors; he had previously normal lungs and no evidence of an immunocompromised state. This was therefore a case of fatal, locally invasive pulmonary aspergillosis due to *A fumigatus*. In the past 30 years only one similar case in an adult has been described,⁴ this having been caused by *Aspergillus niger*. Six almost identical cases caused by *A fumigatus* have, however, been reported in children.⁵ All were in children living in an agricultural environment, where the causative organism is frequently found in large numbers.

In two cases environmental contamination by *A fumigatus* was confirmed.⁵ Heavy environmental exposure to the fungus may be important in our patient in view of his occupation as a gardener, which raises the possibility that this is a hitherto unrecognised occupational lung disorder. The clinical course, as in this case, is one of rapidly progressive bronchopneumonia resulting in death due to respiratory failure. Diagnosis is almost invariably made at necropsy.^{2,5} Postmortem findings in invasive aspergillosis usually take the form of necrotising bronchopneumonia or of haemorrhagic pulmonary infarction. In our case there were pulmonary miliary microabscesses, which are rare, occurring in only 10% of cases²; the appearances are very similar to those of miliary tuberculosis. Invasive aspergillosis may be disseminated by the time of death, but in two thirds of cases the disease is confined to the thorax,² as in our patient. Antemortem diagnosis is difficult. The clinical picture usually leads to a differential diagnosis of atypical pneumonia, miliary tuberculosis, sarcoidosis, and Wegener's granulomatosis. Blood and sputum cultures are generally unhelpful, and in only 30% of cases is the organism isolated from sputum.⁶ In invasive disease *Aspergillus precipitans* may be absent, and more sophisticated serological tests (for example, radioimmunoassay) are highly sensitive, though not widely available. Despite extensive investigation in our patient the only indication of possible infection was the isolation of *A fumigatus* from sputum 24 hours before death. This does not necessarily indicate infection and it was regarded as secondary to multiple antibiotic chemotherapy. Only at necropsy was it clear that *A fumigatus* was the primary pathogen. Successful treatment of invasive aspergillosis is more likely if diagnosis is achieved early and disease is confined to the lungs.¹ The treatment of choice is intravenous amphotericin B with or without flucytosine.⁸

We thank Mrs M T Ludden for her secretarial assistance.

References

- 1 Gordon IJ, Evans CC. *Aspergillus* lung disease. *J R Coll Physicians Lond* 1986;20:206–11.
- 2 Young RC, Bennett JE, Vogel CL, Carbone PP, DeVita VT. Aspergillosis. The spectrum of disease in 98 patients. *Medicine (Baltimore)* 1970;49:147–73.
- 3 Aslam PA, Eastridge CE, Hughes FA. Aspergillosis of the lung—an eighteen year experience. *Chest* 1971;59:28–32.
- 4 Toigo A. Pulmonary aspergillosis. *Am Rev Respir Dis* 1960;81:392–6.
- 5 Strelling MK, Rhaney K, Simmons AR, Thomson J. Fatal acute pulmonary aspergillosis in two children of one family. *Arch Dis Child* 1966;41:34–43.
- 6 Nalesnik MA, Myerowitz RL, Jenkins R, Lenkey J, Herbert D. Significance of *Aspergillus* species isolated from respiratory secretions in the diagnosis of invasive pulmonary aspergillosis. *J Clin Microbiol* 1980;11:370–6.
- 7 Bardana EJ, Gerber JD, Craig S, Cianciull FD. The general and specific humoral immune response to pulmonary aspergillosis. *Am Rev Respir Dis* 1975;112:799–805.
- 8 Sinclair AJ, Rossof AH, Coltman CA. Recognition and successful management of pulmonary aspergillosis in leukaemia. *Cancer* 1978;42:2019–24.