

Treatment of symptomatic pulmonary aspergillomas with intracavitary instillation of amphotericin B through an indwelling catheter

M Jackson, C D R Flower, J M Shneerson

Abstract

Background—The treatment of symptomatic pulmonary aspergillomas can be difficult. One approach has been to deliver antifungal drugs directly into the lung cavity. The use of this method of treatment is described in which an indwelling percutaneous catheter is used which avoids repeated needlings of the cavity and may allow extended treatment on a domiciliary basis.

Methods—Amphotericin B was delivered through indwelling percutaneous intracavitary catheters to treat five symptomatic episodes in four patients with pulmonary aspergillomas.

Results—The treatment was well tolerated by all patients and their symptoms resolved in four of the five episodes. Two patients died, one from an unrelated bronchopneumonia and the other from advanced cachexia. Two patients remain symptom free after eight and 12 months.

Conclusions—Intracavitary administration of amphotericin through an indwelling catheter should be considered for any patient who has troublesome sputum production, haemoptysis, or systemic symptoms attributable to an aspergilloma.

(Thorax 1993;48:928-930)

Pulmonary aspergillomas may develop in cavitating lung disease of any cause. They are most frequent following tuberculosis and sarcoidosis and in the upper lobes. The majority of patients with aspergillomas present to thoracic physicians and surgeons with a productive cough or systemic symptoms such as malaise, weight loss, and fever. An important complication is haemoptysis which may be minor but can be life threatening and is the cause of death in up to 26% of patients.¹

The treatment of symptomatic aspergillomas is difficult. Many patients have poor lung function associated with the underlying disease and are not suitable for surgical resection. There is a significant morbidity and mortality after resection even in patients with reasonable preoperative pulmonary function.² Intravenous amphotericin B is ineffective³ and the role of new oral antifungals, such as itraconazole, remains to be defined.⁴ Several antifungal agents have been delivered topi-

cally, both bronchoscopically and percutaneously, with encouraging results.⁵⁻⁹ This treatment is, however, rarely employed, possibly because of the difficulty that has been experienced in the past with retaining catheters and fears about allergic reactions to and toxicity of amphotericin. We report our experience of the treatment of four patients with symptomatic aspergillomas with intracavitary amphotericin B delivered through indwelling percutaneous catheters.

Methods

The presence of an aspergilloma was suspected from the appearance of the chest radiograph in each case. Conventional tomography (case 1) or computed tomography (cases 2, 3, and 4) was then performed to confirm the presence of the cavity and fungus ball and to map out an access route for percutaneous catheter insertion.

In all four patients the catheter was inserted under local anaesthesia using single plane fluoroscopic guidance. The cavity was punctured percutaneously with an 18 gauge needle through which a guidewire was threaded until its tip lay coiled within the cavity. In cases 1 and 2 an 8 Fr Teflon pigtail was then passed into the cavity over the guidewire which was subsequently removed. In cases 3 and 4 an 8 Fr van Sonnenberg catheter was inserted using the same technique. In all cases the shortest route between skin and cavity was chosen and healthy lung was not transgressed by the catheter. At the end of the procedure the catheter was sutured to the skin and left in place for injection of amphotericin.

An initial dose of 5 mg amphotericin B was administered and the dose was increased each day to 10, 20, 30, 40, and 50 mg delivered daily. The amphotericin B was diluted in 20 ml 5% dextrose in water and injected over 5-10 minutes. The patients were positioned to minimise coughing and to allow the amphotericin to remain in the cavity. Suction was not applied to the catheters. The treatment was continued until the symptoms resolved or the clinical situation precluded further treatment.

Case reports

CASE 1

A 61 year old man with berylliosis presented with malaise, 12.6 kg weight loss, fever,

Department of
Respiratory Medicine
M Jackson
J M Shneerson

Department of
Radiology
C D R Flower

Papworth Hospital,
Papworth Everard,
Cambs CB3 8RE

Reprint requests to:
Dr M Jackson

Received 13 November 1992
Returned to authors
3 March 1993
Revised version received
19 April 1993
Accepted 22 April 1993

increased sputum production, and occasional haemoptysis over a period of 19 months. A chest radiograph and tomograms showed a left apical cavity with a fungal ball. *Aspergillus* precipitins were positive and the fungus was isolated from his sputum and from bronchial washings. A catheter was inserted and he was given a total of 600 mg amphotericin B. His sputum production lessened and fever resolved but he remained cachectic and died three weeks later. Post mortem examination and microbiological investigation of the cavity showed that it was sterile. There were no adverse effects resulting from the amphotericin treatment.

CASE 2

A 79 year old man presented with malaise, weight loss, increased sputum production, and a cutaneous vasculitis. A chest radiograph showed a left apical cavity with a presumed aspergilloma which was confirmed by computed tomography. An underlying cause for the cavitation was not established. He had undergone a partial gastrectomy previously. *Aspergillus fumigatus* was isolated from his sputum and from washings from the cavity. A catheter was inserted and he was given a total of 415 mg amphotericin B. His symptoms were unchanged. He developed an unrelated *Haemophilus influenzae* bronchopneumonia and died three weeks later. A post mortem examination was performed and *Aspergillus fumigatus* was isolated from the fungal ball.

CASE 3

A 48 year old man with pulmonary cavities following tuberculosis presented with symptoms of malaise, increased sputum, fever, and intermittent mild haemoptysis. Investigations revealed positive *Aspergillus* precipitins and the fungus was isolated from his sputum. A chest radiograph showed a right apical cavity with evidence of an aspergilloma on computed tomography. Following insertion of a van Sonnenberg catheter he was given a total of 3 g amphotericin B over nine weeks. The majority of his treatment was on a domiciliary basis. During this period his care was complicated by a superadded infection with *E coli* which was treated with oral amoxycillin. His symptoms completely resolved and he remained well for 18 months, at which time he again experienced increased sputum production, fever, and weight loss. The chest radiograph was unchanged, the precipitins remained positive, and *Aspergillus* was isolated from his sputum. A second catheter was inserted and he was given a total dose of 400 mg amphotericin over eight days. He experienced a mild febrile reaction to the first dose which required no specific treatment. His symptoms again completely resolved and he has remained well during a further 12 months follow up.

CASE 4

A 41 year old man who was an insulin dependent diabetic and had previously been treated for pulmonary tuberculosis presented with

malaise, a productive cough, and weight loss. Investigations revealed no evidence of tuberculous reactivation and a chest radiograph showed a left apical cavity with a typical aspergilloma. His *Aspergillus* precipitins were positive and the fungus was isolated from his sputum. A van Sonnenberg catheter was inserted into the cavity; washings from the cavity at this time also revealed *Aspergillus fumigatus*. He was given daily intracavitary amphotericin to a total dose of 2.4 g with no adverse drug reaction. Follow up computed tomography revealed no change in the size of the cavity and fungus ball. All of his symptoms resolved, however, and he remains well eight months later.

Discussion

Aspergilloma formation is an uncommon event in cavitating lung disease. The 1964-5 BTTA survey of patients with residual tuberculous cavities showed that 14% of 544 such patients had radiological evidence of an aspergilloma.¹⁰ The patients with an aspergilloma were more likely to have symptoms of cough and haemoptysis than those without, but the mortality in the two groups was no different. Treatment of patients with aspergilloma is therefore confined to those with significant haemoptysis, copious productive cough, or systemic symptoms of malaise, weight loss, and fever.

The treatment of such patients is complicated by their underlying lung disease which is often extensive. Surgical resection of aspergillomas is associated with a significant morbidity and mortality. Jewkes *et al*² reported a 7% postoperative mortality rate and 15% developed major complications such as bronchopleural fistula and haemorrhage. Those treated by resection had a better survival rate than those treated medically, but this may have been a result of their better underlying lung function. Varkey and Rose¹¹ reported a 7% mortality rate and a major complication rate of 20%. Patients who were felt to be unfit for resection were submitted for cavernostomy but four out of nine patients treated by this method died.²

A number of medical approaches have been explored, including the successful use of radiotherapy for massive haemoptysis from an aspergilloma.¹² Intravenous amphotericin B has been found to be ineffective³ and is poorly tolerated. Some success has been reported with a new oral antifungal, itraconazole, but only after several months of treatment during which time spontaneous lysis of the aspergillomas may have occurred.⁴ Endobronchial instillation of antifungal agents has been used but the number of reported cases is small.⁵

The feasibility of direct intracavitary treatment has increased with improvements in percutaneous catheter techniques and radiological imaging. Computed tomography provides precise anatomical localisation of the cavity or cavities as well as demonstrating intracavitary masses likely to represent

fungus. In all four of our patients the catheter was inserted under fluoroscopic guidance but could have been placed equally effectively during initial computed tomographic assessment. In our patients the procedure was well tolerated and without complication in all cases.

Intracavitary instillation of sodium iodide solution, nystatin, or amphotericin B paste, and amphotericin B in solution alone or with other agents, has been tried. Krakowka *et al*⁶ reported 20 patients who were treated with a paste containing nystatin or amphotericin B administered by between five and 18 needlings. Haemoptysis lessened in all of the patients and the aspergillomas regressed or disappeared in 11 out of 20 cases. Hargis *et al*⁸ reported six patients treated with intracavitary amphotericin. Four patients received repeated percutaneous injections and two were treated with an indwelling catheter. Four patients improved symptomatically, one did not tolerate the treatment because of repeated systemic reactions, and one did not respond to treatment. Shapiro *et al*⁹ recently reported the successful treatment of six episodes of acute haemoptysis in four patients with intracavitary instillation of amphotericin B, *N*-acetylcysteine, and aminocaproic acid through a percutaneously placed catheter.

The determination of the optimal dose of intracavitary amphotericin and length of treatment is difficult to judge and probably depends both on the load of *Aspergillus* and the accessibility of the fungus to the drug. The chest radiograph is an insensitive method of monitoring treatment as the visible ball may contain only dead *Aspergillus* following treatment as in case 1. *Aspergillus* precipitins are useful to confirm the nature of the condition but conversion to seronegativity occurs after killing of the fungus. Case 3 demonstrates that a standard dose cannot be recommended since this patient relapsed despite having received the largest dose of amphotericin. In practice treatment is continued until the patient's symptoms have fully resolved and is extended for a further, arbitrary, period.

The use of an indwelling percutaneous

catheter has several advantages. It allows delivery of antifungal treatment directly into the cavity containing the aspergilloma and allows a full course of treatment without repeated needlings of the cavity. The insertion of the catheter is performed easily under local anaesthesia and we have not experienced toxic side effects from the amphotericin. In contrast to surgical resection there is no loss of lung tissue and the treatment can be repeated if necessary. Once treatment has begun it can be continued on a domiciliary basis. In all five instances the insertion procedure was tolerated without complication and the instillations were not associated with any significant systemic reaction.

Our experience confirms that intracavitary amphotericin through an indwelling catheter is an effective and well tolerated treatment and we suggest that it should be considered for any patient who has troublesome sputum production, haemoptysis, or systemic symptoms attributable to an aspergilloma.

- 1 Glimp RA, Bayer AS. Pulmonary aspergilloma: diagnostic and therapeutic considerations. *Arch Intern Med* 1983;143:303-8.
- 2 Jewkes J, Kay PH, Paneth M, Citron KM. Pulmonary aspergilloma: analysis of prognosis in relation to haemoptysis and survey of treatment. *Thorax* 1983; 38:572-8.
- 3 Hammerman KJ, Sarosi GA, Tosh FE. Amphotericin B in the treatment of saprophytic forms of pulmonary aspergillosis. *Am Rev Respir Dis* 1974;109:57-62.
- 4 Campbell JH, Winter JH, Richardson MD, Shankland GS, Banham SW. Treatment of pulmonary aspergilloma with itraconazole. *Thorax* 1991;46:839-41.
- 5 Ramirez R J. Pulmonary aspergilloma: endobronchial treatment. *N Engl J Med* 1964;271:1281-5.
- 6 Krakowka P, Traczyk K, Walczak J. Local treatment of aspergilloma of the lung with a paste containing nystatin or amphotericin B. *Tubercle* 1970;51:184-91.
- 7 Adelson HT, Malcolm JA. Endocavitary treatment of pulmonary mycetomas. *Am Rev Respir Dis* 1968;98:87-92.
- 8 Hargis JL, Bone RC, Stewart J, Rector N, Hiller FC. Intracavitary amphotericin B in the treatment of symptomatic pulmonary aspergillomas. *Am J Med* 1980;68: 389-94.
- 9 Shapiro MJ, Albelda SM, Maycock RL, McLean GK. Severe haemoptysis associated with pulmonary aspergilloma: percutaneous treatment. *Chest* 1988;94: 1225-31.
- 10 British Tuberculosis Association. *Aspergillus* in persistent lung cavities after tuberculosis. *Tubercle* 1968;49:1-11.
- 11 Varkey B, Rose HO. Pulmonary aspergilloma—a rational approach to treatment. *Am J Med* 1976;61:626-31.
- 12 Shneerson JM, Emerson PA, Phillips RH. Radiotherapy for massive haemoptysis from an aspergilloma. *Thorax* 1980;35:953-4.