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Intracavitary Aspergilloma: Transthoracic Percutaneous Injection of Amphotericin Gelatin Solution[1]

For aspergillomas in patients with fibrocavitary lung disease, surgery is often not recommended. Injection or lavage of the cavities with solutions of potassium iodide or antifungal agents has had varying success and requires repeated sessions because of nonretention of the therapeutic agent within the cavity. In three patients with four aspergillomas, the authors used fluoroscopic or computed tomographic (CT) guidance to inject amphotericin in gelatin as a liquid that solidifies within the cavity at body temperature. The patients were followed up with serial chest radiography or CT. The mixture was successfully instilled in every case. Three of the four aspergillomas completely resolved within 3 months or less, with no evidence of recurrence at follow-up of 6–18 months. The remaining aspergilloma decreased in size, but the patient needed pneumonectomy because of recurrent hemoptysis within 6 months of amphotericin injection. Transthoracic instillation of a liquid mixture of amphotericin and gelatin that solidifies rapidly at body temperature may be useful as a one-step treatment for aspergillomas.

Index terms: Aspergillosis, 60.2056, 60.254 • Lung, infection, 60.2056, 60.254 • Interventional procedures, 60.1291

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See also the article by Giron et al (pp 825–827) in this issue.

ASPERGILLOMAS are a well-known complication of cavitary lung disease (1–4). They most frequently occur in patients with previous tuberculous infection. The main complication is hemoptysis, which develops in 50%–95% of cases and may be fatal. Ideally, these patients undergo surgical resection of the affected segment of lung; this is often technically difficult, however, and may be contraindicated because of limited respiratory reserve or other problems (3–5). Because of this, nonsurgical therapies such as systemic antifungal therapy and endobronchial or intracavitary instillation of antifungal agents have been attempted; all have had limited or mixed success (1–5). One of the disadvantages of medical therapy has been the necessity for repeated treatment due in large part to nonretention of antifungal agents within the cavity. We report our early experience with transthoracic intracavitary instillation of an amphotericin B and gelatin mixture that is liquid at slightly warmer than body temperature but solidifies at body temperature after instillation within the cavity. This solidification permits retention of the antifungal agent locally, thereby minimizing systemic effects as well as preventing rapid dissipation of the drug.

MATERIALS AND METHODS

Three patients underwent treatment with this method. Two had a previous history of tuberculosis. One patient had undergone right upper lobectomy and radiation therapy for incompletely resected bronchogenic carcinoma 2 years previously. The cavity was presumed to be due to radiation therapy. A total of four cavities containing large aspergillomas were treated: two in the right upper lobe and two in the left upper lobe (Table). All the patients were male and ranged in age from 42 to 78 years, with an average of 54 years. In all patients, pretreatment radiographs demonstrated classic findings of a soft-tissue opacity within the cavity outlined by a crescent of air (Fig 1). Aspergilloma was diagnosed on the basis of clinical findings, serial radiographs, and positive results of the *Aspergillus* precipitin assay. Findings of repeated cultures of sputum for *Aspergillus* were available in two cases. Two patients also had undergone preoperative computed tomography (CT) (Fig 2) and magnetic resonance imaging with gadolinium contrast enhancement. Injection was guided with fluoroscopy in three cavities and with CT in one cavity (Fig 3).

The amphotericin B gelatin preparation was prepared as follows: Six grams of oxoid laboratory standard gelatin was dissolved in 8½ mL of sterile water by means of a hot water bath at 40°C. Then 15 mg of amphotericin B was dissolved in the mixture. Immediately before injection, the mixture was drawn up within a syringe that had been warmed to 40°C in the hot water bath. In each instance the procedure was performed in the radiology department by a radiologist (P.L.M., R.N.R.). Before the amphotericin B gelatin mixture was drawn into the syringe, needle position within the cavity was confirmed with fluoroscopy, CT, or both. In each case the needle tip was placed within the mycetoma.

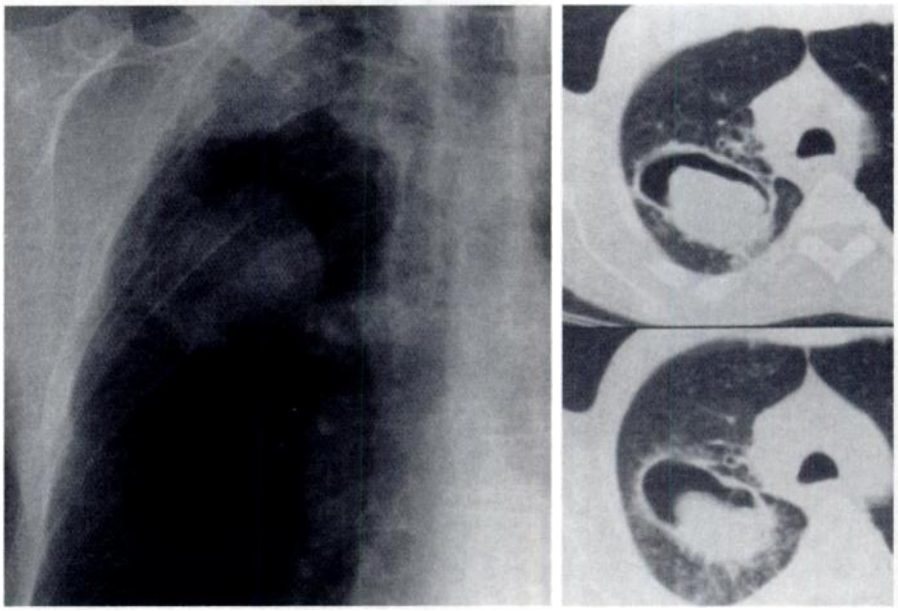
To facilitate injection of the viscous mixture a large-bore needle of either 16 or 18 gauge was utilized. The syringe was hooked up directly to the needle to minimize the transit time for the gelatin mixture. Because the mixture is relatively viscous and solidifies rapidly, it is imperative that it be injected rapidly. As soon as the mixture was completely injected or when the needle had clogged because of hardening of the gelatin, the needle syringe assembly was removed and postprocedural chest radiographs were obtained to determine whether pneumothorax was present. All patients were followed up by means of serial radiography, and two patients underwent follow-up CT 2 months after the procedure (Fig 4). Follow-up radiographs obtained 6–18 months after the procedure were available. Patients were assessed for toxicity by following the complete blood cell count and renal function (creatinine levels and blood urea nitrogen levels). All patients gave informed consent for the procedure and were receiving no other therapy for their aspergillomas.

RESULTS

Needles were readily placed in the mycetomas in the cavities in each instance. In two instances the entire volume (approximately 10 mL) of the amphotericin B gelatin mixture was injected. In two instances only approximately half the volume could be injected before gelatin hardening precluded further injection through the clogged needle. In one instance the gelatin mixture was inadvertently heated to 42°C and a large portion of the gelatin material was expectorated. In all patients the procedure was tolerated satisfactorily. One patient had a pneumothorax that required drainage with a small-bore chest tube, and one patient had a small and localized pneumothorax that did not require evacuation. A minor degree of hemoptysis was noted in two instances. All patients demonstrated substantial diminution in the size of the mycetoma within 3 weeks after injection. By 3 months the mycetoma completely disappeared in three cases and decreased from 6.5 × 5 cm to 4.5 × 3 cm in the remaining case. The last case was in the patient who developed an aspergilloma cavity after partial right upper lobectomy and radiation therapy. No patients showed evidence of systemic toxicity.

Cavity and Aspergilloma Dimensions at Time of Therapy

Location	Cavity Size (cm)	Aspergilloma Size (cm)
Right upper lobe	7.0 × 5.0 × 4.5	6.5 × 5.0 × 4.0
	8.0 × 6.5 × 6.0	5.0 × 4.5 × 4.5
Left upper lobe	5.5 × 4.5 × 4.0	4.0 × 3.5 × 3.5
	4.0 × 4.0 × 3.0	3.5 × 3.0 × 3.0



1. 2.

Figures 1, 2. **(1)** Posteroanterior chest radiograph obtained in a 50-year-old man demonstrates a large cavity in the right upper lung with a rounded tissue opacity outlined by air. Marked pleural thickening and fibrosis are appreciated at the apex of the right hemithorax. The images in Figures 2–4 were obtained in the same patient as in Figure 1. **(2)** CT scans of the chest with lung windows show two adjacent sections through the cavitary lesion in the right upper zone seen on the chest radiograph in Figure 1. These scans confirm the presence of a large cavity containing a dependent, large, soft-tissue lesion representing the aspergilloma. A crescent of air is appreciated anteriorly and laterally. The cavity has a moderately thick, slightly irregular wall.

DISCUSSION

Intracavitary aspergillomas are a common complication in patients with cavitary granulomatous disease of the lung and can become a significant and life-threatening problem (1–5). A large proportion of these patients will have episodes of hemoptysis, some of which may be massive (ie, > 300 mL in 24 hours) and fatal in up to 26% in some series of patients with aspergilloma (2–5). Although bronchial artery embolization is helpful in the palliative treatment of hemoptysis, without definitive therapy of the aspergilloma, hemoptysis will almost certainly recur. Even in the absence of aspergillomas, recurrence of massive bleeding after successful embolization occurs in more than 20% of patients at 6 months (6–8). Ideally, patients in whom surgery can be tolerated should undergo removal of the affected segment of the lung for definitive treatment. Surgery, unfortunately, is often difficult because of massive scarring and vascularization of the walls of the affected tissue and is not always possible. In addition, many of these patients have diminished respiratory reserve. Because of this, a large proportion of these patients are poor surgical candidates who have substantial postoperative morbidity and mortality rates that may be in excess of 8% (3,5).

Attempts at medical or nonsurgical therapy for these disorders have been undertaken (1,2,4). Systemic treatment with intravenous antifungal agents is not effective and has a substantial risk of nephrotoxicity and hepatic toxicity (9). The prevalence of resolution of aspergillomas in these patients is similar to the approximately 10% rate of spontaneous lysis (10). Either transthoracic or endobronchial injection of agents such as sodium iodide, amphotericin B, nystatin, and other drugs has been utilized with variable success. Hargis et al used multiple percutaneous injections of amphotericin in saline solution to treat their patients with up to a total dose of 500 mg (4). Four of six patients were able to complete the

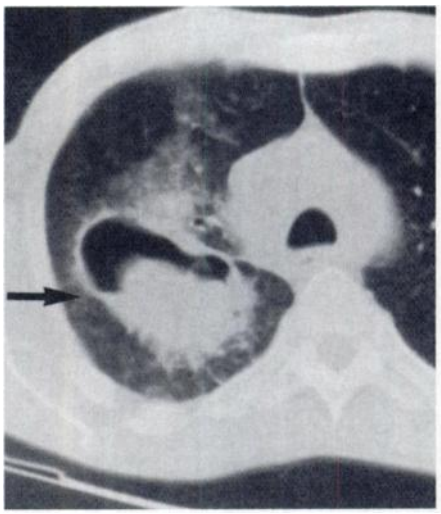
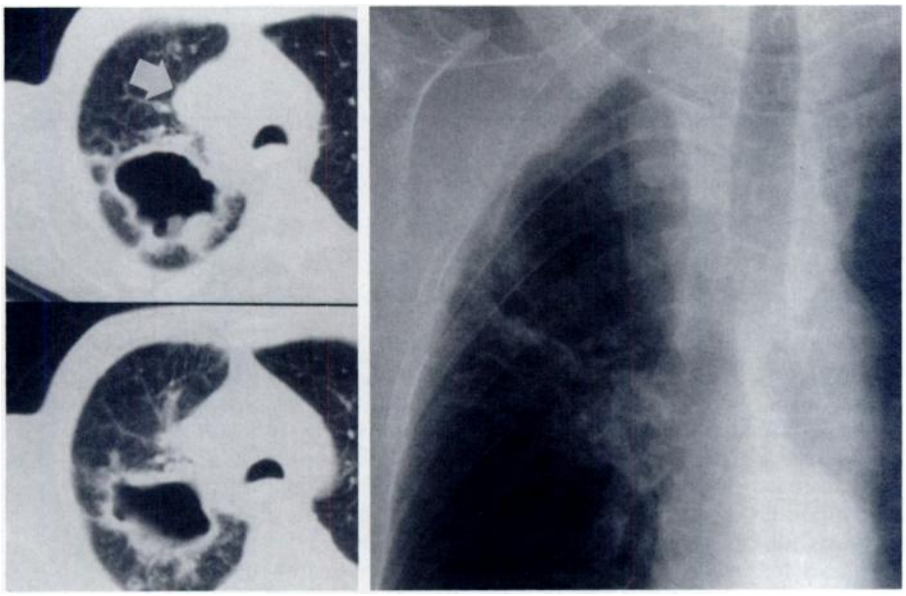


Figure 3. Single CT section through the upper right lobe was obtained after injection of the amphotericin B–gelatin mixture into the mycetoma with an anterior approach. A fluid level is present within the cavity (arrow). Air-space disease is present anterior to the cavity; this finding is consistent with some parenchymal hemorrhage along the course of the needle track.



a. b.

Figure 4. (a) CT scans through the right upper lobe 5 months after the injection of amphotericin gelatin show that a large cavity remains in the right upper lobe. The mycetoma is markedly decreased in size, with only a small amount of debris seen in the dependent portion of the cavity posteriorly. The mediastinal nodes enlarged during the interval (arrow). (b) Posteroanterior chest radiograph obtained 9 months after injection shows no evidence of residual mycetoma.

series of injections and showed complete resolution of their aspergillomas. One patient demonstrated systemic toxicity to the amphotericin. Others have utilized transthoracic small-bore catheters introduced into the cavity to facilitate irrigation of the cavity with these antifungal agents (1,2). All of the patients showed resolution of their aspergillomas after repeated irrigation over several days with antifungal agents and mucolytics. Although these treatments may be successful, they do require multiple sessions of treatment and are therefore inconvenient. In addition, multiple doses of the drug must be administered, increasing the risk of systemic toxicity.

The instillation of a mixture that solidifies at body temperature keeps the drug within the cavity, therefore precluding the necessity for multiple drug instillations and also possibly decreasing systemic toxicity. Gelatin is already utilized as an embolic agent and is known to be safe. It is also inexpensive and is easily liquefied at near physiologic temperatures. The use of the liquid gelatin mixture posed minor technical problems. A solution that is too warm can be rapidly expectorated from the cavity (which occurred in one instance), while a solution that is too cool can solidify before a substantial amount can be injected. With practice we found it possible to balance these two problems and successfully inject an adequate amount of medication into the cavities. Since the drug stays within the cavity, a relatively small amount could still theoretically result in a high local concentration. It is therefore possible that less than the 50 mg that we injected could be adequate. This may be the reason that the patient in whom a large portion of the gelatin mixture was expectorated still had resolution of the mycetoma. It is presumed that at least a small quantity of the gelatin mixture coated the aspergilloma and the cavity and that the retained drug coating these structures was sufficient to destroy the mycetoma.

Although our patient experience is relatively small, transthoracic percutaneous injection of amphotericin gelatin solution appears to be an effective one-step treatment of aspergillomas. This treatment may be considered in the management of mycetomas and hemoptysis in patients in whom surgery is not recommended. ■

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References

1. Lee KS, Kim YH, Bae WK. Percutaneous intracavitary treatment of a giant aspergilloma (letter). AJR 1990; 154:1346.
2. Shapiro MJ, Albelda SM, Mayock RL, McLean GK. Severe haemoptysis associated with pulmonary aspergilloma. Chest 1988; 96:1225–1231.
3. Al-Majed SA, Ashour M, El-Kassimi FA, et al. Management of post-tuberculous complex aspergilloma of the lung: role of surgical resection. Thorax 1990; 45:846–849.
4. Hargis JL, Bone RC, Stewart J, Rector N, Hiller FC. Intracavitary amphotericin-B in the treatment of symptomatic pulmonary aspergillomas. Am J Med 1980; 68:389–394.
5. Shirakusa T, Ueda H, Saito T, Matsuba K, Kouno J, Hirota N. Surgical treatment of pulmonary aspergilloma and aspergillus empyema. Ann Thorac Surg 1989; 48:779–782.
6. Hickey NM, Peterson RA, Leech JA, Chambers RJ, Shamiji PM. Percutaneous embolotherapy in life-threatening hemoptysis. Cardiovasc Intervent Radiol 1988; 11:270–273.
7. Uflacker R, Kaemmerer A, Pico P, et al. Bronchial artery embolization in the management of hemoptysis: technical aspects and long-term results. Radiology 1985; 157: 637–644.
8. Stoll JF, Bettmann MA. Bronchial artery embolization to control hemoptysis: a review. Cardiovasc Intervent Radiol 1988; 11:263–269.
9. Ikemoto H. Treatment of pulmonary aspergilloma with amphotericin B. Arch Intern Med 1965; 115:598–601.
10. Hammerman KJ, Saiosi GA, Tosh FE. Amphotericin B in the treatment of saprophytic forms of pulmonary aspergillosis. Am Rev Respir Dis 1974; 109:57–89.