

Case report - Thoracic general

Management of postpneumonectomy Aspergillus empyema extending into the thoracic wall: a plea for radical surgery and caution when using liposomal amphotericin B

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Abstract

Semi-invasive aspergillosis is a rare disease leading to severe complications even in fully immunocompetent patients. The therapeutic role of systemic and intrapleural antifungal agents remains not well known. We report herein the case of a 54-year-old woman who developed Aspergillus empyema invading the thoracic wall and subcutaneous tissues after completion pneumonectomy for aspergilloma. She initially was treated conservatively with systemic and intrapleural amphotericin B without any success and developed a severe anaphylactic reaction to intravenous liposomal amphotericin B (Ambisome®). She then underwent an open-window thoracotomy with intrathoracic transposition of a latissimus dorsi muscle flap and was started on itraconazole therapy. The thoracostomy was closed after 6 months and the patient is doing well without any signs of recurrent infection after 3 years.

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1. Introduction

The spectrum of pulmonary aspergillosis varies considerably, ranging from allergic bronchopulmonary aspergillosis to invasive disease depending on the immune status of the patient and the underlying lung condition [1].

Severe complications such as thoracic wall invasion are rare.

We present an immunocompetent woman who developed an empyema with Aspergillus fumigatus extending through the thoracic wall to the subcutaneous tissues following completion pneumonectomy for aspergilloma. We initially elected to treat her with a conservative approach including systemic and intrapleural amphotericin B. However, the patient did not improve and required radical surgery with thoracostomy and intrathoracic latissimus dorsi muscle flap transposition. Interestingly, the patient also developed a severe anaphylactic shock to a unique and low dose of intravenous liposomal amphotericin

B, whereas systemic and intrapleural conventional amphotericin B did not cause any reaction.

2. Case history

A 54-year-old woman suffered from severe and recurrent tuberculosis as a child requiring a left upper lobectomy in 1965. Since then she had a normal life. In 1999, she developed severe productive cough and dyspnea. Bronchoscopy showed pus in the left main bronchus and repeated cultures revealed Aspergillus fumigatus. Serum precipitins as well as specific IgE (3.7 kU/l) were strongly positive for Aspergillus fumigatus. The patient had a normal blood count including white cells repartition; serum immunoglobulins levels and cellular immune response as assessed by Multitest Mérieux (Institut Mérieux, Lyon France) were in the normal range. CT-Scan showed aspergilloma and bronchiectasis of the remaining left lower lobe (Fig. 1). No improvement occurred despite 2 months therapy of oral itraconazole (400 mg/day). In July 2000, we performed a decortication and completion left pneumonectomy.

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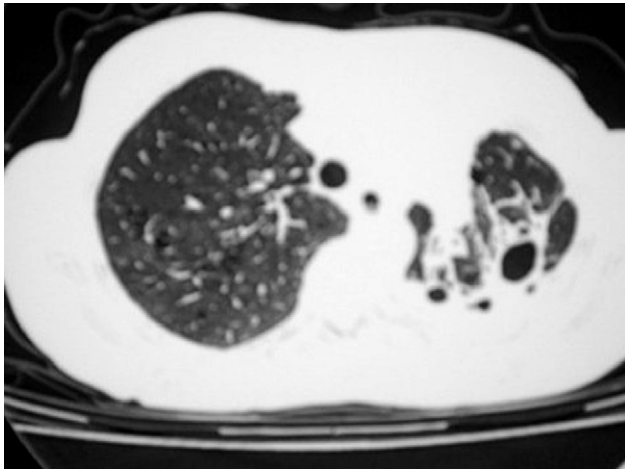


Fig. 1. CT-scanner showing the aspergilloma in the left upper thoracic cavity.

Histology confirmed the presence of aspergilloma and bronchiectasis in the left lower lobe. Itraconazole therapy was pursued. Four days after surgery, she developed a tiny bronchopleural fistula (BPF) of the left stump diagnosed by bronchoscopy. The left pleural cavity was drained. The cultures remained sterile. After 3 months, while she still was under itraconazole therapy, the patient developed a large subcutaneous abscess under the left breast. A CT-scan showed a communication between the abscess and the left pleural cavity through the thoracic wall. Cultures from the subcutaneous abscess and the pleural cavity grew only *Aspergillus fumigatus*. Postpneumonectomy empyema with semi-invasive aspergillosis extending into the thoracic wall and subcutaneous tissue was diagnosed.

Parenteral infusion of liposomal amphotericin B (Ambisome®; 1 mg/kg over 1 h) was started in order to prevent the systemic side effects of amphotericin B such as gastrointestinal or renal function impairment. However, within 1 min after the first pleural administration, the patient developed severe bronchospasm, tachypnea, generalized cutaneous rash and hypotension (systolic blood pressure of 50 mmHg), requiring intravenous adrenaline to control the severe anaphylactic reaction.

We therefore decided to perform a continuous irrigation-drainage of the pleural cavity and the subcutaneous tissue with conventional amphotericin B (25 mg/day) associated with intravenous conventional amphotericin B (50 mg/day). No itraconazole was used concomitantly because of the theoretical but likely antagonism between azoles and polyenes [2]. Conventional amphotericin B was well tolerated and no allergic reaction was noted.

The *Aspergillus fumigatus* infection persisted despite local and systemic amphotericin therapy for 8 weeks. Therefore, an open window thoracostomy (Fig. 2) with intrathoracic transposition of a latissimus dorsi muscle flap was performed according to a technique previously described [3]. The pleural cavity was packed daily with wet dressing of diluted povidone-iodine (Betadine) and oral



Fig. 2. Thoracostomy allowing prolonged drainage of the left thoracic cavity.

itraconazole therapy was started and maintained for 6 months. The clinical status of the patient improved considerably and subsequent repeated cultures remained negative. The thoracostomy was then closed 6 months later. After 3 years of follow-up, the patient is perfectly well and did not show any sign of recurrent *Aspergillus* infection.

3. Discussion

Aspergillus species can produce a wide range of pulmonary disorders [1,4]. Semi-invasive aspergillosis or chronic necrotizing aspergillosis is a chronic process with local invasion of the lung tissue but without vascular invasion. It is usually seen in patients with mild immunosuppression like diabetes mellitus, low-dose corticosteroid therapy, and poor state of nutrition or connective tissue disorders.

Classical symptoms are fever, cough and weight loss over many months.

We had no evidence of any immunocompromized state in our patient. She did not show any evidence of any debilitating condition apart from an old and quiescent history of tuberculosis. Her asthma was very mild and well controlled by β_2 -agonists without using any systemic or topical corticosteroids.

However, after the completion of pneumonectomy for aspergilloma, she developed severe complications such as empyema and semi-invasive aspergillosis. Very few cases of aspergillosis have been reported with extension through the thoracic wall into the subcutaneous tissues in immunocompetent patients [5,6].

The treatment of semi-invasive aspergillosis after pneumonectomy is not well established [7–9]. Antifungal therapy is recommended but the value of intrapleural antifungal agents and the optimal choice between itraconazole, amphotericin B or a combination of both, remains unknown. In our experience, we were unable to control the *Aspergillus* infection using

intrapleural and systemic amphotericin B therapy. Therefore, in postpneumectomy aspergillus empyema, we would recommend a rapid and aggressive surgical approach with open-window thoracostomy associated with intrathoracic muscle flap transposition to close a potential bronchopleural fistula and plumb the pleural space. This approach should help to shorten the duration of the Aspergillus infection and increase the chances of cure [5,6,10].

Unexpectedly, our patient experienced an anaphylactic shock under liposomal amphotericin B therapy, whereas conventional amphotericin B was well tolerated. We should keep this potential complication in mind when using liposomal amphotericin B and always use a testing dose under careful supervision before starting this expensive form of therapy.

In conclusion, postpneumectomy empyema with semi-invasive *Aspergillus fumigatus* is a dreadful complication, which requires aggressive therapy including open window thoracostomy, intrathoracic muscle transposition, and systemic antifungal therapy. Systemic and intrapleural antifungal agents alone appear ineffective and may potentially be complicated by severe anaphylactic reaction when liposomal amphotericin B is used.

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